Uveitis and Allied Disorders

16

Contents

16.1 Introduction

This is a broad and varied group of conditions which have commonality in clinical presentation and features. They often provide a diagnositic challenge with shared investigative methods.

16.2 Non-infectious Uveitis of the Posterior Segment

Fig. 16.1 Use the slit lamp beam to detect cells in the vitreous in inflammatory conditions. Check for cells in any odd presentation of macular ERM or retinal detachment in case there is an underlying inflammatory cause

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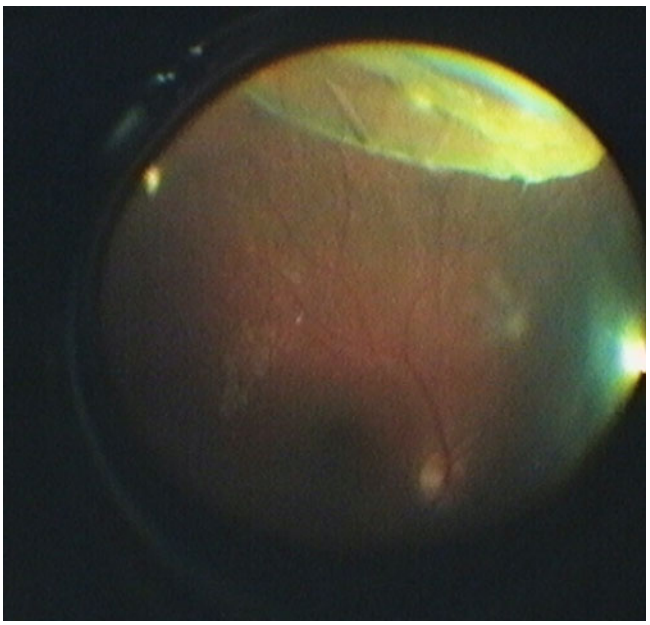

Fig. 16.2 Indentation reveals snow banking in this patient with intermediate uveitis

Fig. 16.4 This composite picture shows a pattern of Eales' disease. These patients can produce neovascularisation and vitreous haemorrhage

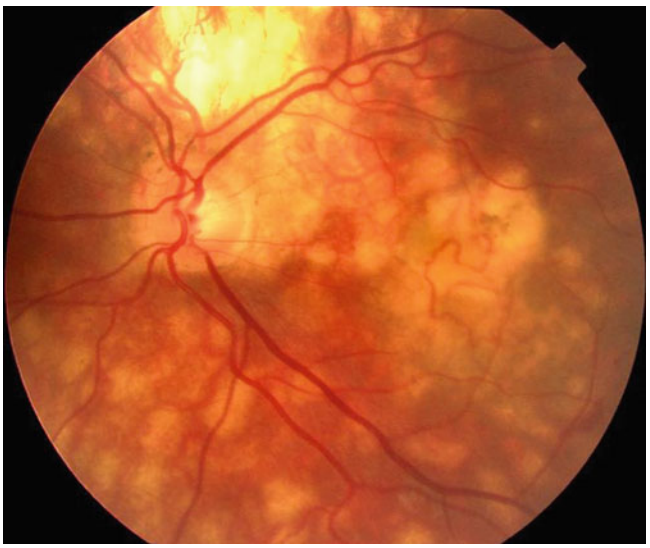

Fig. 16.3 Sarcoidosis is a very common cause of posterior uveitis

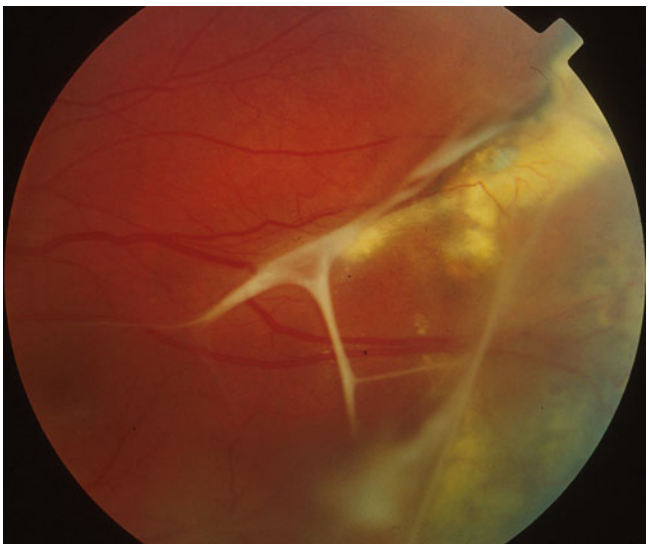

Fig. 16.5 This patient with idiopathic uveitis has subretinal exudation and epiretinal membranes

The variety of possible presentations of uveitis of the posterior segment makes it difficult to generalise on the surgical approach (Mieler et al. 1988; Eckardt and Bacskulin 1992; Nolle and Eckardt 1993). The conditions that the surgeon may encounter, depending on the racial mix and geographical location, include:

- Intermediate uveitis
- Sarcoidosis
- Uveitis of juvenile chronic arthritis
- Behcet's disease
- Idiopathic vasculitis including Eales' disease
- Birdshot chorioretinopathy
- Vogt–Koyanagi–Harada syndrome
- Sympathetic uveitis
- Takayasu's arteritis

In the Western population, the commonest presentations are likely to be intermediate uveitis, sarcoidosis and juvenile chronic arthritis. Although often relatively controllable with systemic therapy, those patients with more severe

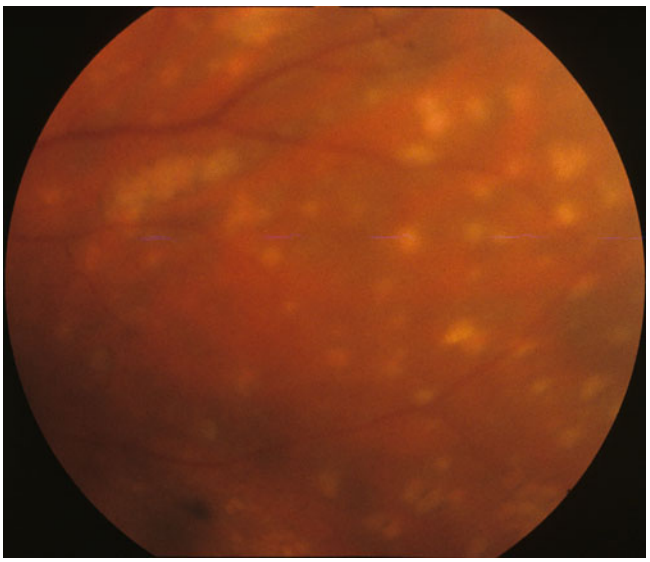

Fig. 16.6 Sympathetic uveitis is a rare cause characterised by white retinal spots, sometimes attributed to the pathological feature of Dalen–Fuch's nodules

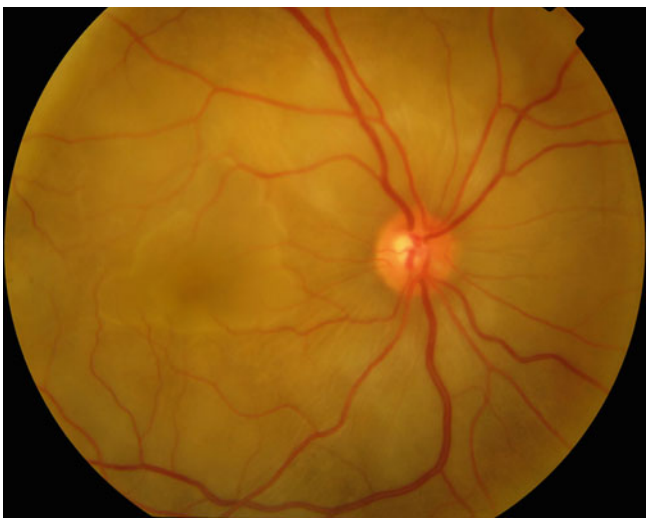

Fig. 16.7 A patient with exudative RD from Vogt–Koyanagi–Harada syndrome

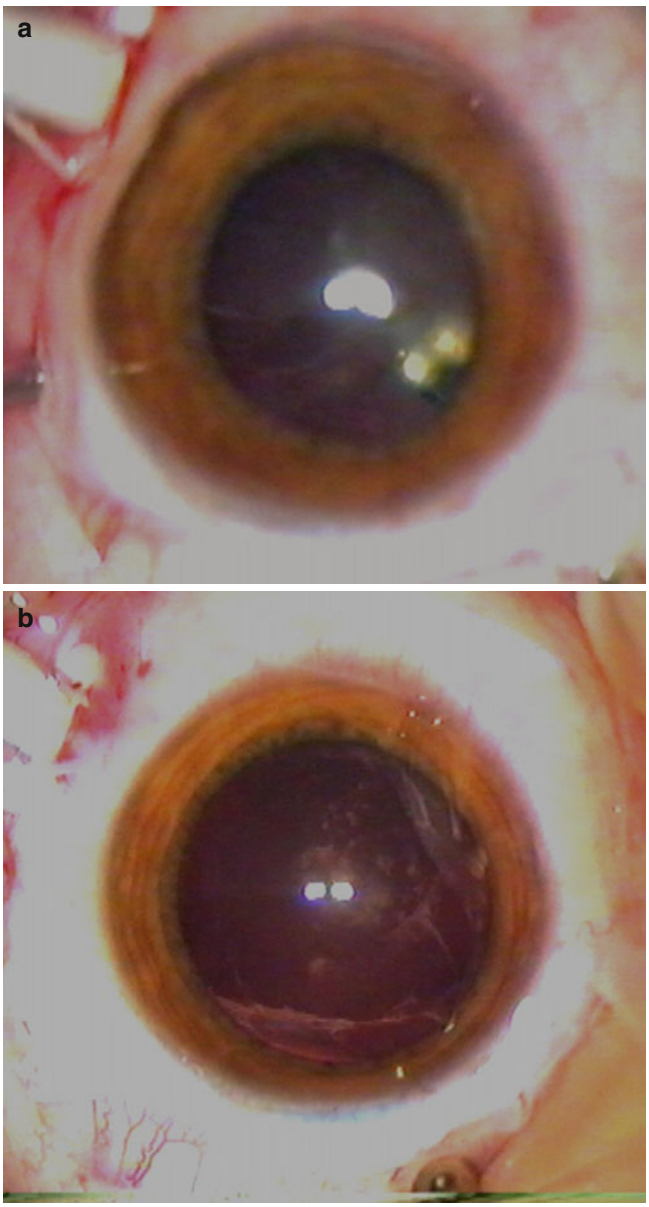

Fig. 16.8 (**a**, **b**) In patients with uveitis, vitreous with debris and cells can be adherent to the posterior lens surface obscuring the view for the surgery. With careful aspiration with the vitreous cutter, the vitreous can be teased off of the posterior lens without damaging the posterior capsule

disease may require vitreoretinal intervention for the following reasons:

- Diagnostic confirmation
- Vitreous opacification
- Rhegmatogenous retinal detachment (RRD)
- Tractional retinal detachment (TRD)
- Exudative retinal detachment
- Cystoid macular oedema (CMO)
- Epiretinal membrane
- Hypotony

The vitreous may become opaque because of the presence of cellular deposits, proteinaceous infiltration and degeneration of the gel structure. The inflammatory process can cause shrinkage of the gel which in the presence of vitreoretinal adhesion may produce either TRD or RRD (Mieler et al. 1988; Bovey and Herbort 2000; Heiligenhaus et al. 1994). In patients with intermediate uveitis, cystoid macular oedema may account for between 40 and 60 % of eyes with poor vision (Scott et al. 2003; Dugel et al. 1992). Ultimately phthisis bulbi from hypotony is the most severe end point from these inflammatory conditions (Kokame et al. 2001). It causes a catastrophic visual loss and even a cosmetically unacceptable eye, often in young patients.

16.2.1 Vitreous Opacification

Removal of the vitreous cells and debris in the vitreous gel may restore vision in patients with uveitis of the posterior segment (Eckardt and Bacskulin 1992; Mieler and Aaberg 1992; Heimann et al. 1992; Kaplan 1992; Diamond and Kaplan 1979). Intermediate uveitis may be complicated by vitreous haemorrhage that can be treated successfully by vitrectomy (Potter et al. 2001). Many of these patients are young and have attached PHM, which will require removal, but the PHM may be difficult to detach because of vitreoretinal adhesions. Postoperatively the eye may produce inflammation requiring systemic immunosuppressive cover over the peroperative period. Visual recovery is often limited because of the presence of optic atrophy or retinal damage particularly from CMO (Verbraeken 1996; Waters et al. 2000). Some surgeons claim that removal of the gel reduces the ability of the eye to hold inflammatory mediators and thereby reduces recurrence of inflammation in the long term. Evidence for this remains uncertain (Bovey and Herbort 2000). Others argue that improvement following surgery is a result of the removal of vitreous opacity rather than any influence on the inflammatory process (Mieler et al. 1988). Also reduction in medical treatment after surgery has been blamed for a rebound of inflammation 3–6 months later. Therefore, PPV is not recommended routinely in these patients but is reserved for the treatment of the vitreoretinal complications.

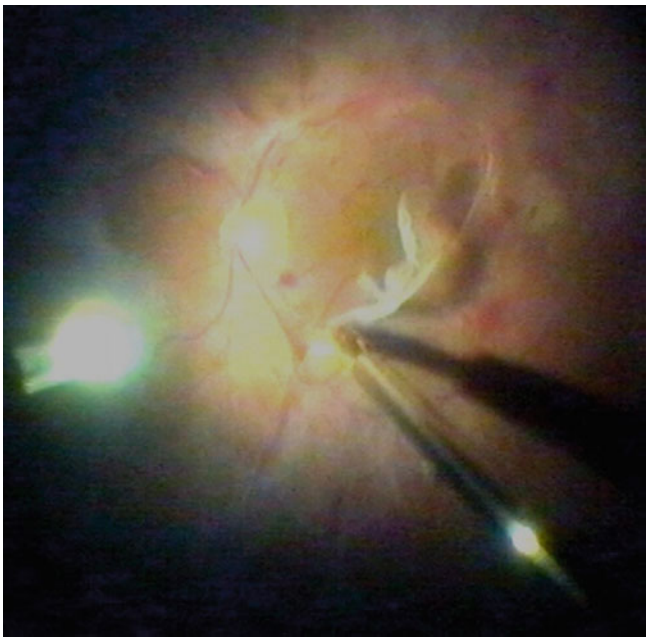

Fig. 16.9 In this patient with uveitis, a secondary epiretinal membrane has formed and has been removed during vitrectomy

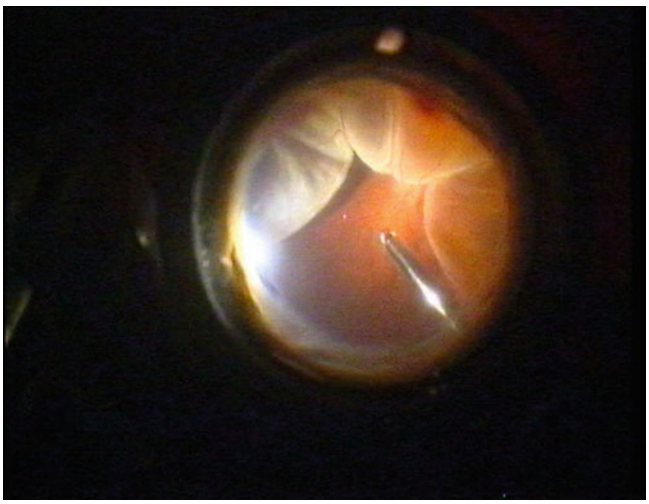

Fig. 16.10 In a patient with suspected exudative retinal detachment, heavy liquids can be inserted onto the posterior pole and gradually expanded. If there are no retinal breaks, there is route for escape of subretinal fluid, and the retina will bulge forwards anteriorly in bullae around the top of the heavy liquids. If a retinal break is present, then sclera may be identified and the subretinal fluid will spontaneously leave the subretinal space and the retinal detachment will resolve

Retinal vasculitis can produce ischaemia and a neovascular response associated with vitreous haemorrhage. PPV can be used to relieve traction to prevent recurrent haemorrhage and clear the visual axis. Unlike diabetic retinopathy, panretinal photocoagulation is not universally required.

16.2.2 Retinal Detachment

When TRD is associated with neovascularisation or fibrosis, delamination and dissection of the membranes are required. A vitreoschisis, as seen in diabetic retinopathy (Chap. 9), may be present and must be recognised to allow appropriate dissection under the plane of the PHM to aid delamination. Unfortunately TRDs are often associated with severe subretinal exudation in uveitic eyes, and visual recovery is often poor.

Rarely patients present with TRD without neovascularisation or preretinal fibrosis; a smooth elevation of the retina is seen. PPV and peeling of the PHM will suffice, allowing the retina to settle without need to drain SRF.

RRD may occur from PVD formation and can be dealt with by routine means (see Chap. 6) whilst being aware of the possibility of exacerbation of the uveitis.

Exudative RD may be encountered and diagnosed by shifting fluid and the absence of retinal tears, traction and epiretinal fibrosis (despite a long-standing duration of retinal detachment) (Gaun et al. 2002). Beware that the patient does not have uveal effusion syndrome. If immunosuppressive therapy does not reattach the retina, PPV a retinotomy to drain the SRF or an external drainage may help. During the surgery, the exudative nature of the retinal detachment can be confirmed by inserting heavy liquids onto the posterior

retina. This will displace SRF anteriorly where it is trapped (because there is no retinal hole to allow drainage) and forms a tight ring bulla which overhangs the heavy liquid. Removal of the heavy liquid reveals a return of the retinal detachment to its previous configuration, confirming no loss of SRF. Perform a small and peripheral retinotomy to drain SRF and laser the retinotomy. Alternatively bend a needle as for an external drain (see DACE procedure, Chap. 6) whilst viewing the retina internally via PPV and indent the sclera gently with the 'heel' of the bend in the needle to locate its position. Locate the needle into an area of high SRF (fill the posterior pole with heavy liquid to create a ring bulla), then rotate the needle to insert the point through the scleral and choroid to commence drainage. With small-gauge surgery, the needle can be inserted through the conjunctiva. Fill with long-acting gas or silicone oil. If the uveitis is then controlled, return of the retinal detachment is unlikely.

16.2.3 Cystoid Macular Oedema

Steroid injections into the vitreous cavity can reverse CMO in uveitis. However, the chronic nature of these conditions causes a return of the CMO after the steroid has been cleared from the eye (Antcliffe et al. 2001). Slow-release steroid implants or injections may overcome this difficulty and are now available. For example, slow-release dexamethasone pellets can be injected as an outpatient procedure; they have an effect for 3–6 months similar to intravitreal triamcinolone but appear to have less chance of an IOP rise (Haller et al. 2010a, b). PPV has been performed to try to relieve traction on the macula to resolve cystoid macular oedema (Dugel et al. 1992; Verbraeken 1996; Aylward 1999) because the vitreous is more often attached than not in patients with CMO (Davis et al. 1992). Others have examined the severity of cystoid macular oedema and found both improvement (Heiligenhaus et al. 1994; Tranos et al. 2006) and persistence of the complication following vitrectomy (Diamond and Kaplan 1978; Priem et al. 1993). Separating the response to vitrectomy from the natural history of the condition and from the effects of concomitant therapies is difficult because randomised studies have not been done.

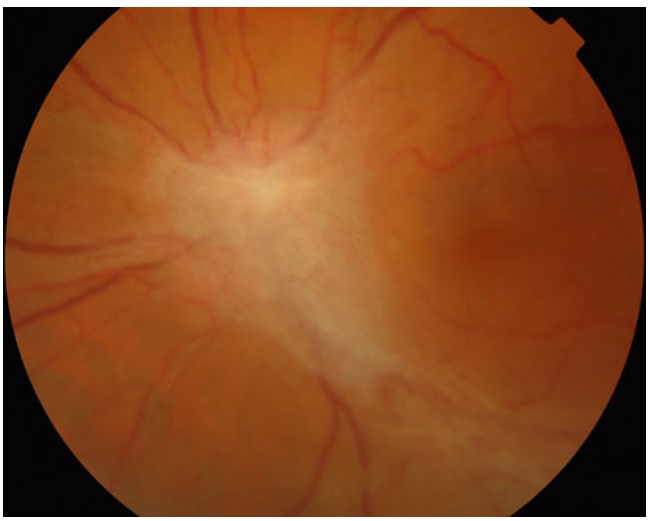

Fig. 16.11 A papillitis has stimulated an ERM which is wrinkling the fovea

16.2.4 Hypotony

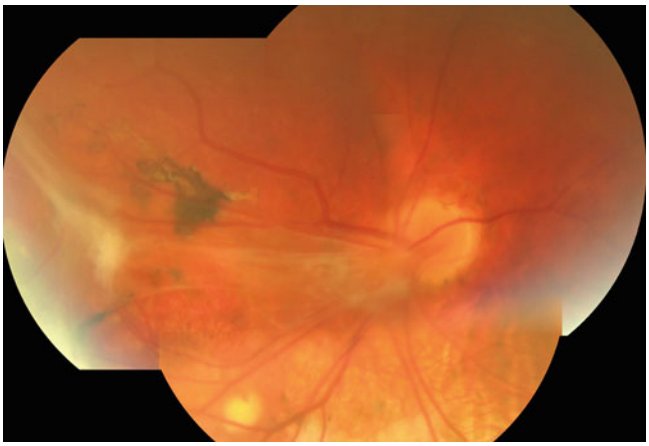

Fig. 16.12 A fold through the macula in a patient with severe panuveitis. The risk of putting the eye into hypotony must be considered before operating on any eye with panuveitis

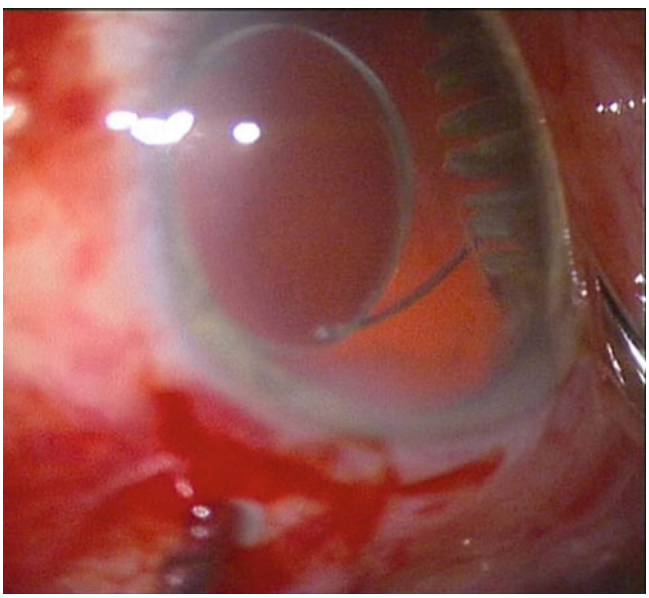

Fig. 16.13 A normal ciliary body

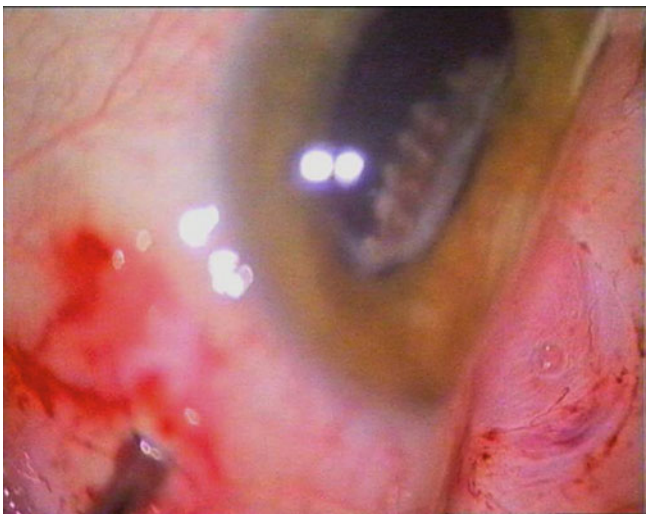

Fig. 16.14 White caps on the ciliary processes from uveitis

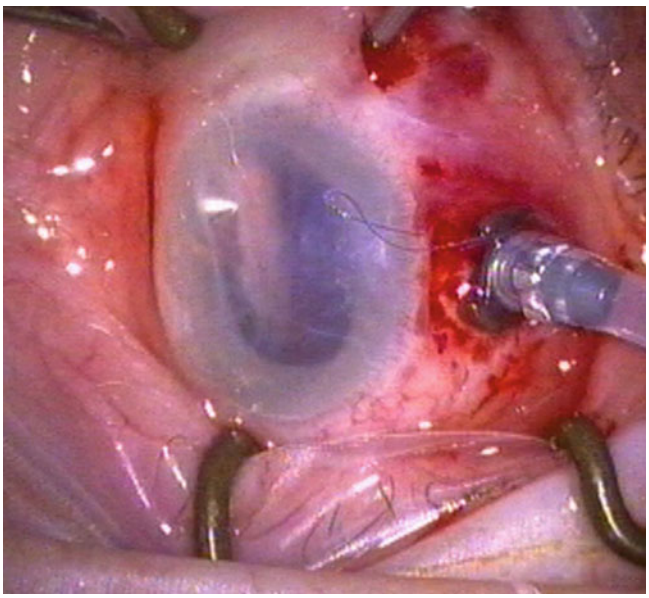

Fig. 16.15 Complete absence of ciliary processes in hypotony from uveitis

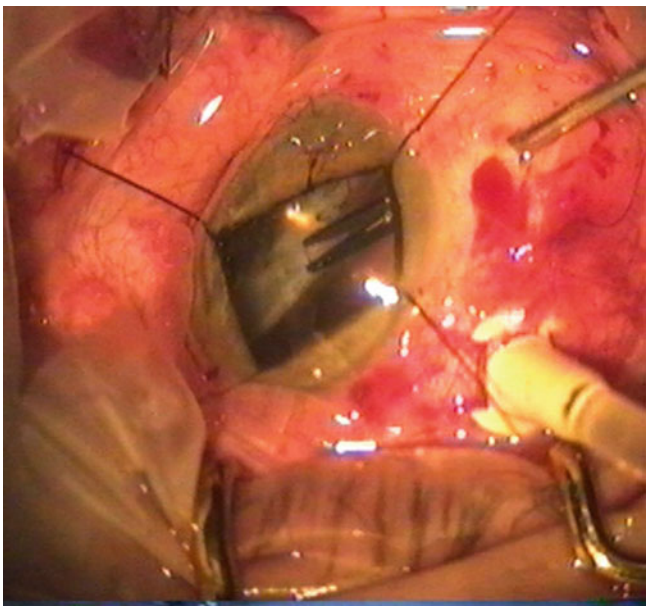

Fig. 16.16 Ciliary body membrane formation

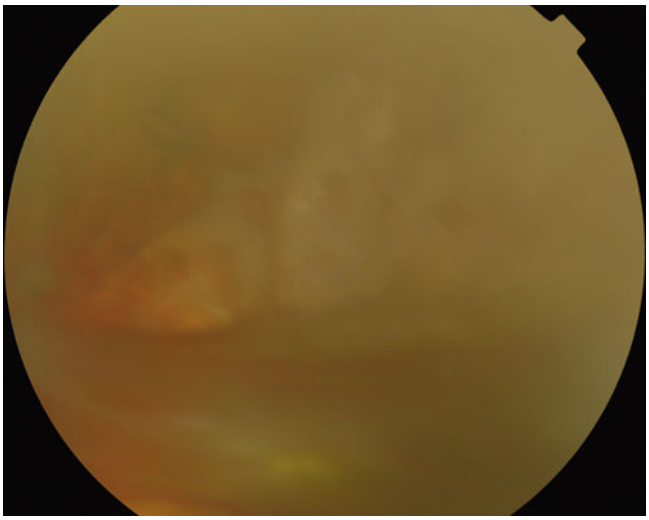

Fig. 16.17 The folds in the posterior layers of the eye are a precursor to phthisis in this patient with panuveitis. The surgeon may choose to fill the eye with silicone oil to retain a cosmetically acceptable globe size and shape and vision of low grade

Hypotony occurs in these eyes because the ciliary body becomes involved in the uveitic process.

Causes of ciliary body failure:

Traction

Atrophy

Detachment

Vitrectomy has been used to try and relieve traction on the ciliary body in hypotony (Kaplan 1992). Inspection of the ciliary body with dissection of any tractional membranes has been performed only in a few patients and is as yet of uncertain worth especially as often the ciliary processes are atrophic and may be non-functional. Insertion of hyaluronic to provide a temporary IOP rise has been employed. Silicone oil can be used for a more prolonged effect and to prevent severe shrinkage of the size of the eye if hypotony persists (Morse and McCuen 1991). Long-term results of these interventions are unknown.

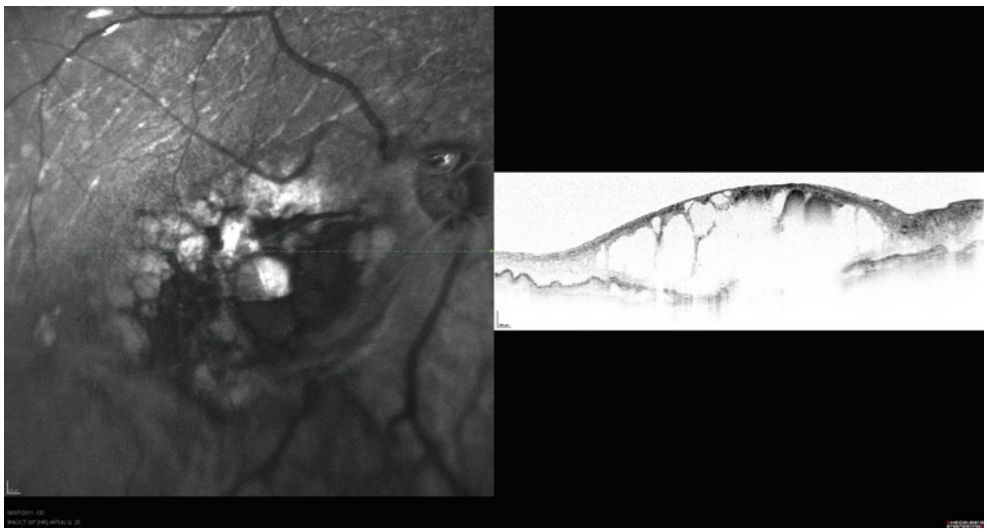

Fig. 16.18 A hypotonous eye is likely to have CMO

Drug	Mode of action	Typical adult maintenance dosage	Severe systemic complications
Prednisolone	Corticosteroid	1–15 mg	Peptic ulceration Myopathy Osteoporosis Adrenal suppression Cushing's syndrome
Azathioprine	Antiproliferative	1–3 mg/kg daily	Myelosuppression Especially those with low thiopurine methyltransferase activity
Mycophenolate mofetil	Antiproliferative	1 g twice daily	Leucopenia Opportunistic infections
Methotrexate	Antimetabolite (inhibits dihydrofolate reductase)	7.5 mg weekly	Myelosuppression Mucositis Pneumonitis 7.5
Ciclosporin	Calcineurin inhibitor	5 mg/kg daily	Nephrotoxicity
Tacrolimus	Calcineurin inhibitor		Neurotoxicity Cardiomyopathy
Infliximab	Tumour necrosis factor activity inhibition	3 mg/kg every 2 months by IV infusion	Infections Heart failure Hypersensitivity Blood disorders
Rituximab	Tumour necrosis factor activity inhibition	1 g every 2 weeks by IV infusion	Infections Heart failure Hypersensitivity Blood disorders
Etanercept	Tumour necrosis factor activity inhibition	25 mg twice weekly by subcutaneous injection	Infections Heart failure Hypersensitivity Blood disorders

16.2.4.1 Diagnostic Confirmation

Uveitic syndromes may occasionally be difficult to discriminate from other causes of posterior infiltration such as infection and neoplasm. Polyclonal white cells are seen on cytology with a CD4/CD8 ratio of at least 4 (Davis et al. 2005). A significant number of patients with uveitis do not have a definitive diagnosis. Only 66 % of cases of anterior uveitis are associated with clinical and laboratory abnormalities which lead to a definitive diagnosis increasing to 85 % in posterior uveitis (Priem et al. 1993). Laboratory examination of the vitreous is particularly indicated when unusual or non-characteristic presentations occur.

Biopsy of the vitreous by needle aspiration may be effective in postoperative endophthalmitis (Han et al. 1999) where the vitreous is liquefied by the infection but may not be appropriate in non-infectious uveitis. Use of a vitreous cutter is recommended because of the greater incidence of vitreoretinal adhesion in uveitic patients increasing the risk of retinal detachment or tear (Verbraeken 1996). Many of these patients are young and likely to have non-syneretic vitreous gel increasing the likelihood of a 'dry tap' with a needle. In some cases, vitrectomy is the ideal; in addition to providing a vitreous sample, vitrectomy may allow visualisation of the fundus, allowing characteristic features of the disease process to be recognised and hence revealing a supplementary diagnosis.

16.2.5 The Vitreous Biopsy

Use transconjunctival 23 or 25 gauge if possible inserted at 4 mm from the corneal scleral limbus; if not available, create the usual 20-gauge sclerotomy opening inferotemporally (see Chap. 2).

A table of immunosuppressive agents that can be used in the treatment of uveitis.

Insert the cutter and visualise in the eye.

Maintain the IOP with a squint hook providing scleral indentation whilst employing the cutter to extract the vitreous to beyond the three-way tap (inserted on the first junction of the aspiration tubing), providing approximately 0.5 ml of vitreous.

Remove the cutter and reinflate the eye with any intravitreal drug administration, for example, antibiotics, whilst relieving the pressure on the squint hook.

Sew up the sclerotomy and conjunctiva if 20 gauge.

Remove the sample from the tubing to send to the laboratory. Take an anterior chamber sample via a paracentesis as required.

16.2.6 Sampling at the Beginning of a PPV

If a small sample is required at the beginning of a PPV, the sample needs to be 'dry', that is, not diluted with the infusion fluid; therefore,

- Insert the infusion cannula, but do not switch it on.
- Create a superior sclerotomy and remove the vitreous whilst applying pressure with the squint hook.
- Remove the cutter and extract the sample.
- Switch on the infusion and release the pressure with the squint hook.
- Continue the PPV.

At the end of the PPV after closing one sclerotomy and with the infusion switched off, insert any intravitreal injections, close the other sclerotomy and then remove the infusion cannula.

16.2.6.1 Special Situations

- If a large sample (2 ml) is required, infuse the eye with heavy liquids which will fall to the back of the eye maintaining its IOP whilst allowing removal of the vitreous and a dry tap (Quiroz-Mercado et al. 2005).
- For some conditions (e.g. *Candida* and bacterial endophthalmitis for culturing or lymphoma for cytometry), it is worth sending the 'washings', vitreous diluted with infusion fluid in the vitrectomy equipment aspiration cassette, to the laboratory.
- Note: If you are inserting gas or silicone oil and you want to use intravitreal drugs, insert the drugs into the vitreous cavity just before inserting the tamponade agent. This ensures that the drugs are of the correct dosage (diluted in 4 ml of fluid in the vitreous cavity). The concentration will remain the same in the thin layer of remaining fluid after fluid/oil or fluid/gas exchange.

Table 16.1 Adult drug dosages (these are guidelines only, the administration of the medications can vary in different institutions)

Disorder	Drug	Dosage	Route of administration
Candida endophthalmitis	Amphotericin B	0.005 mg in 0.1 ml	Intravitreal
	Fluconazole	200–400 mg/day for 3 weeks	Oral
	Flucytosine (often combined with Fluconazole to avoid resistance)	50–150 mg/kg/day divided doses (reduce in renal impairment)	Intravenous infusion
	Voriconazole	400 mg b.d. loading dose, 200 mg b.d.	Oral
CMV retinitis	Gancyclovir	1.5–2.0 mg/0.1 ml	Intravitreal
HSV and VZV acute retinal necrosis (treatment in the acute phase)	Foscarnet	2.4 mg/0.1 ml	Intravitreal
	Aciclovir	10 mg/kg t.d.s for 10 days, monitor renal function	Intravenous infusion
	Valaciclovir	1 g t.d.s. for 10 days	Oral
HSV and VZV acute retinal necrosis (prevention of infection in the fellow eye)	Valaciclovir	300 mg t.d.s. for 3 months	Oral
Bacterial endophthalmitis	Vancomycin	2 mg/0.2 ml	Intravitreal
	Ceftazidime (used in combination)	2 mg/0.2 ml	
Intraocular inflammation or cystoid macular oedema	Triamcinolone	2 mg/0.05 ml	Intravitreal
	Triamcinolone	40 mg	Subtenons
Lymphoma	Methotrexate	0.4 mg/0.16 ml	Intravitreal
Toxoplasmosis chorioretinitis	Pyrimethamine	100 mg stat., then 25 mg b.d. for 3 weeks	Oral
	Sulfadiazine	1 g b.d. for 3 weeks	
	Folinic acid	15 mg 2× weekly	
	Prednisolone (used in combination)	60 mg tapering,10 mg every 5 days	
	Clindamycin	300 mg q.d.s. for 3 weeks	Oral
Peroperative prophylaxis	Vancomycin	10 mg/2 ml (1 g in 20 ml water = 50 mg in ml, take 1 ml dilute in 9-ml water)	Infusion bottle
		Inject 2 ml	

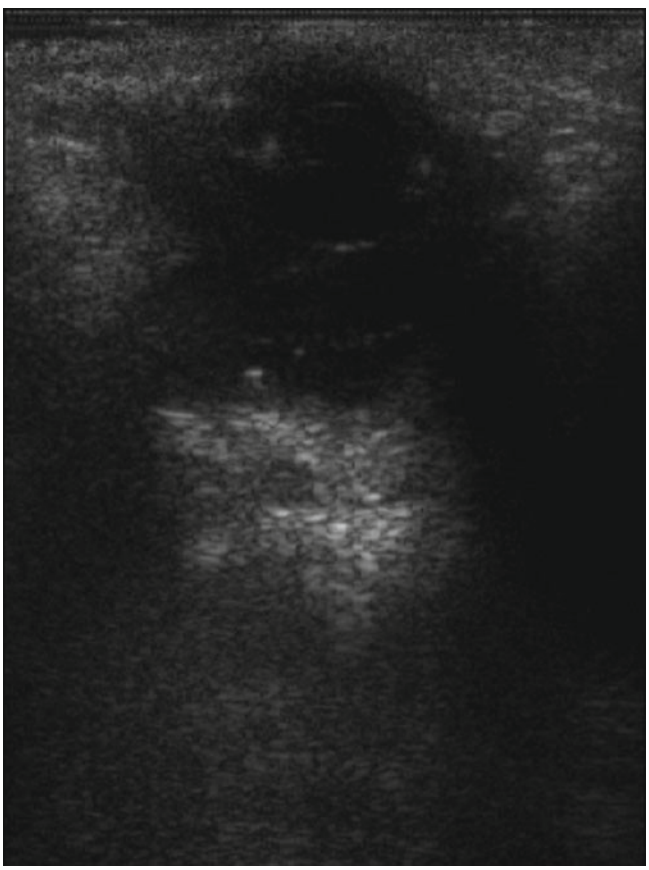

Fig. 16.19 An ultrasound of a patient with panuveitis with an intraocular pellet of slow-release steroid

16.3 Acute Retinal Necrosis

16.3.1 Clinical Features

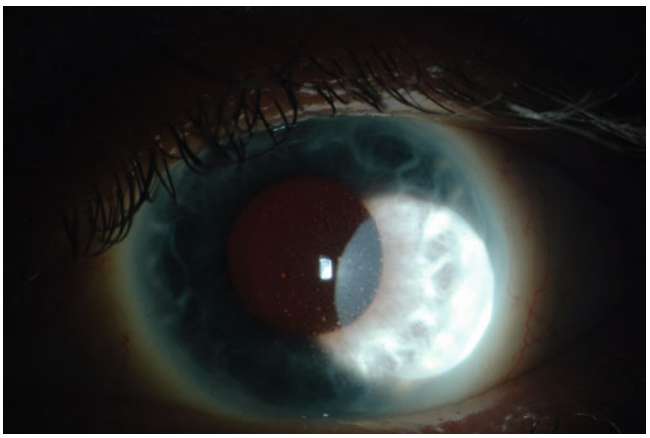

Fig. 16.20 Small 'spidery' keratotic precipitates are often associated with virus-associated uveitis. In this patient, cytomegalovirus was detected on PCR analysis of an aqueous sample

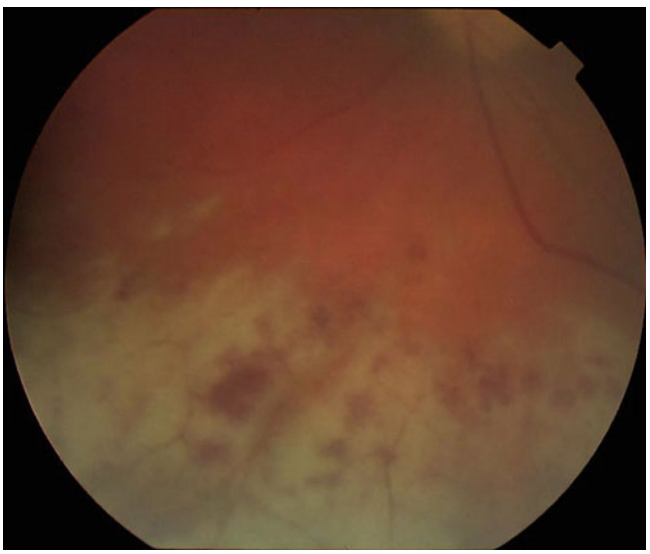

Fig. 16.21 The advancing edge of acute retinal necrosis is visible in this patient. Retinal detachments are extremely common in this condition

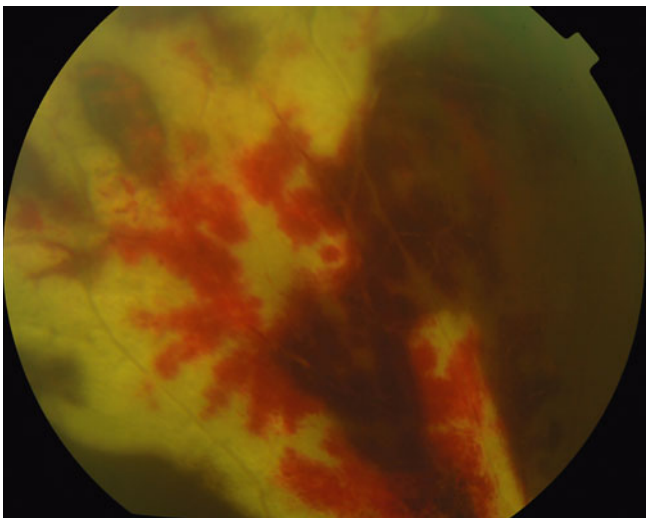

Fig. 16.22 Acute retinal necrosis is characterised by peripheral white lesions with a crenated edge advancing centrally sometimes with retinal haemorrhaging

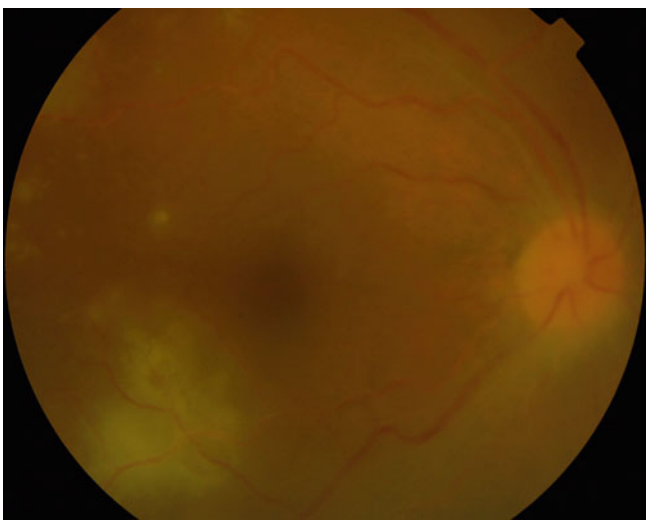

Fig. 16.23 When the infection reaches the optic nerve, the vision drops severely

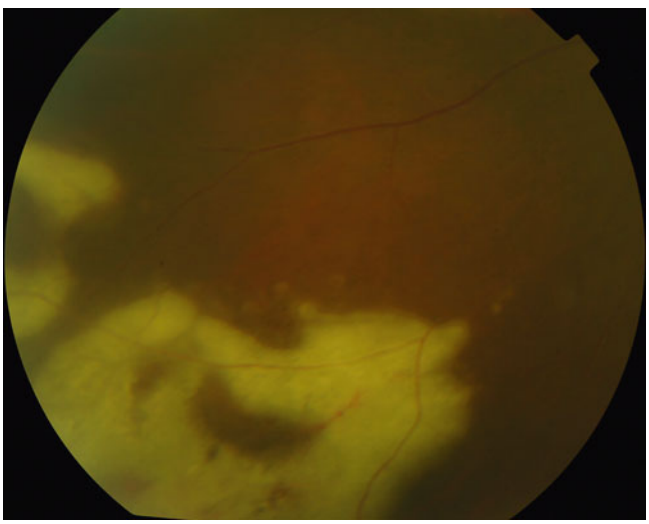

Fig. 16.24 ARN after commencement of steroid therapy

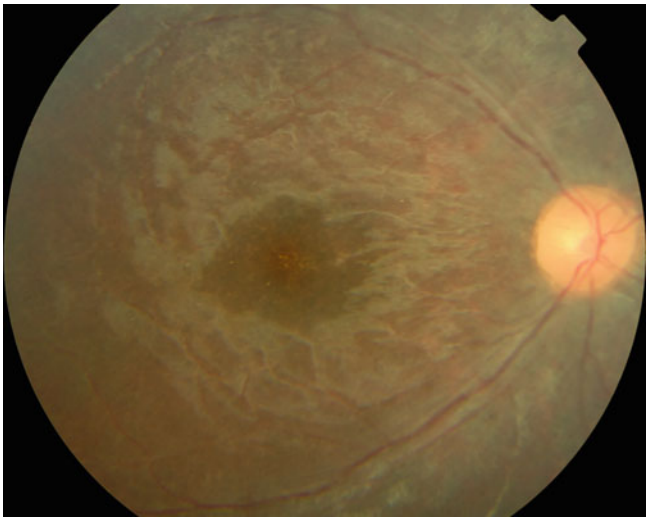

Fig. 16.25 A 5-year-old boy developed an atypical acute retinal necrosis without retinal infiltration but with retinal vasculitis in both eyes a few months after chicken pox. Vision was perception of light in both eyes

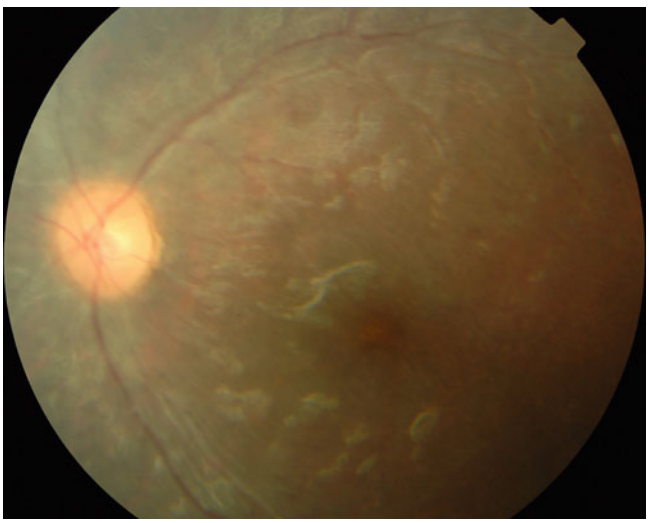

Fig. 16.26 See previous figure

Viral infections of the retina cause a mixed arteritic and infiltrative retinitis. The causative viruses are commonly of the herpes simplex family (Akpek et al. 1999a).

Herpes simplex 1 is commoner in the young age group (Rahhal et al. 1996; Lewis et al. 1989).

These patients may have a history of cold sores.

Herpes zoster is commoner in the elderly (Freeman et al. 1986; Bali et al. 2003; Zambarakji et al. 2002) and can be associated with herpes zoster ophthalmicus (Nakanishi et al. 2000) and chicken pox (Culbertson et al. 1991).

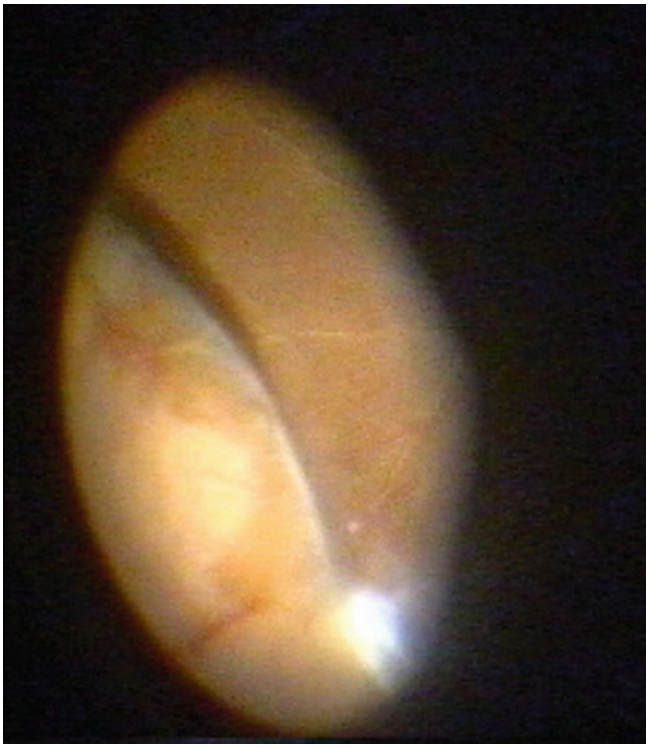

Fig. 16.27 A discrete-edged large retinal break is seen on indentation in this patient with acute retinal necrosis

Herpes simplex 2 infections can also occur especially in children (Rahhal et al. 1996; Markomichelakis et al. 2001; Rappaport and Tang 2000).

Epstein–Barr virus can rarely be detected but is often considered to be a coincidental finding (Hershberger et al. 2003).

Patients are generally not immunocompromised, but herpes zoster is implicated in both ARN (Hershberger et al. 2003; Weinberg and Lyon 1997) and progressive outer retinal necrosis in AIDS patients (Purdy et al. 2003; Austin 2000; Moorthy et al. 1997; Perez-Blazquez et al. 1997; Pavesio et al. 1995; Margolis et al. 1991) and the immunocompromised.

There is a significant risk of bilateral disease (Ezra et al. 1995; Martinez et al. 1992) with fellow eye involvement even years later (Matsuo et al. 1987) and a long-term risk of encephalitis (Ahmadieh et al. 1991; Bloom et al. 1977).

The retina has the appearance of peripheral haemorrhage and infiltration, which spread posteriorly to involve the macula, but the presentation has variable severity (Bloom et al. 1977). The retina may become moth eaten, and retinal detachment is common up to 50 % (Carney et al. 1986). In severe presentations, exudative retinal detachment can occur (Duker et al. 1990). Patients have been described with giant retinal tears (Topilow et al. 1982), retinal neovascularisation (Wang et al. 1983) and peripheral retinal pigment epithelial tears (Fox and Blumenkranz 1993). Proliferative vitreoretinopathy is common.

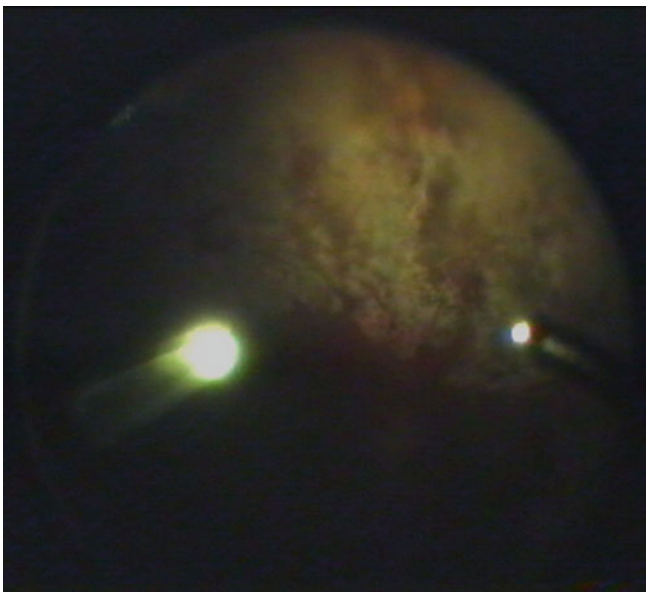

Fig. 16.28 In this patient, a retinal detachment has followed after acute retinal necrosis. Sometimes discrete tears are identifiable, but often the retina is 'moth eaten', and the exact location of breaks is difficult

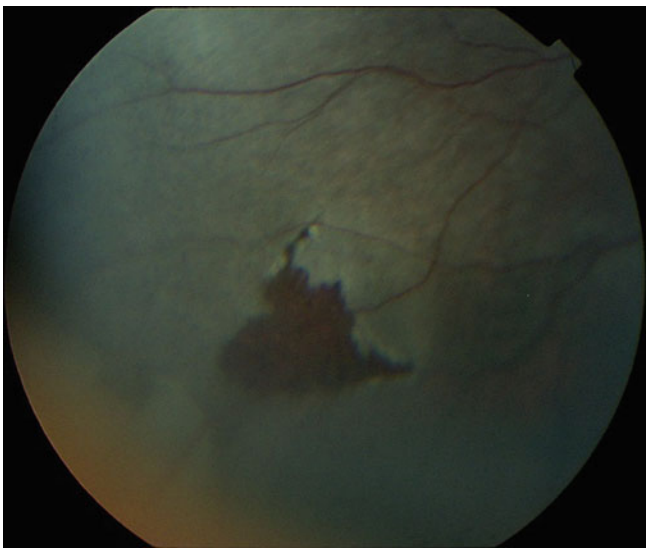

Fig. 16.29 Progressive outer retinal necrosis occurs in the immunocompromised individuals with herpes simplex or zoster infection of the retina. Retinal tears and detachment are common

16.3.2 Surgery

Table 16.2 Difficulty rating for surgery for ARN

Difficulty rating	High
Success rates	Low
Complication rates	Moderate
When to use in training	Late

16.3.2.1 For Diagnosis

The clinical pattern can be useful in diagnosis, but vitreous biopsy is mandatory. A vitreous sample of 0.2 ml is usually sufficient to allow the detection of the virus on polymerase chain reaction (PCR) with a high yield of positive results of 60–80 % (Gerling et al. 1992; Verbraeken and Libert 1995).

16.3.2.2 For Treatment

Systemic antiviral therapy is given over a period of months to try to prevent involvement of the second eye and encepha-

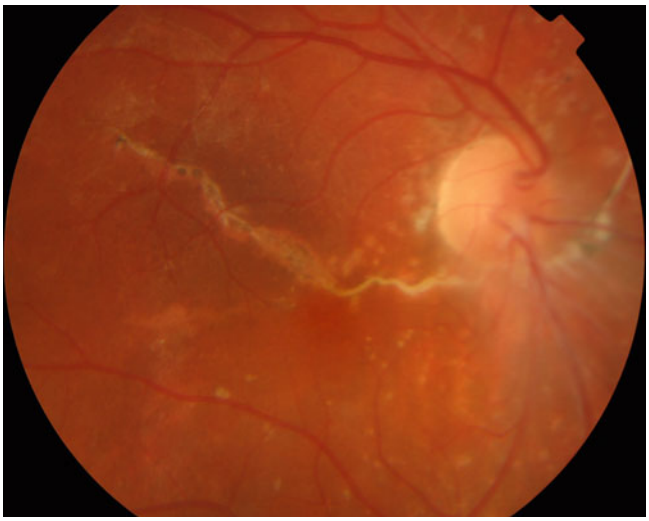

Fig. 16.30 This teenager suffered RRD after ARN; his retina is shown 4 years after the surgical repair reattached without silicone oil in situ with evidence of damage and a subretinal fibrous band

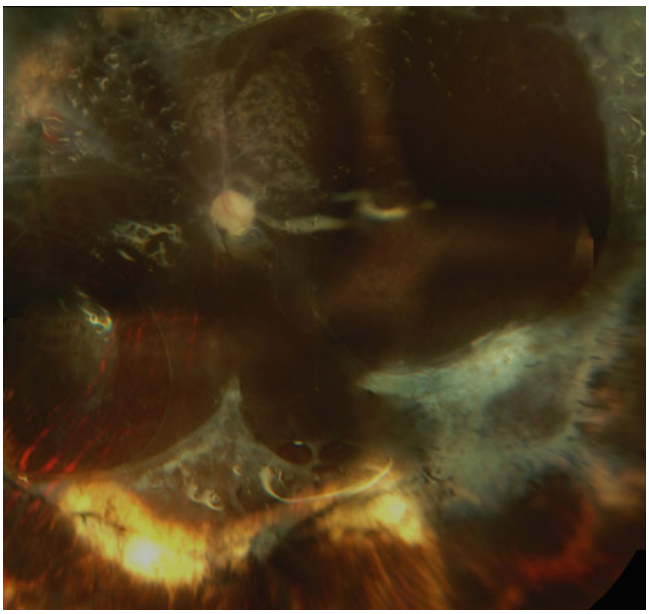

Fig. 16.31 Progressive outer retinal necrosis is shown postoperatively with oil in situ to retain a reattached retina with hand movement vision

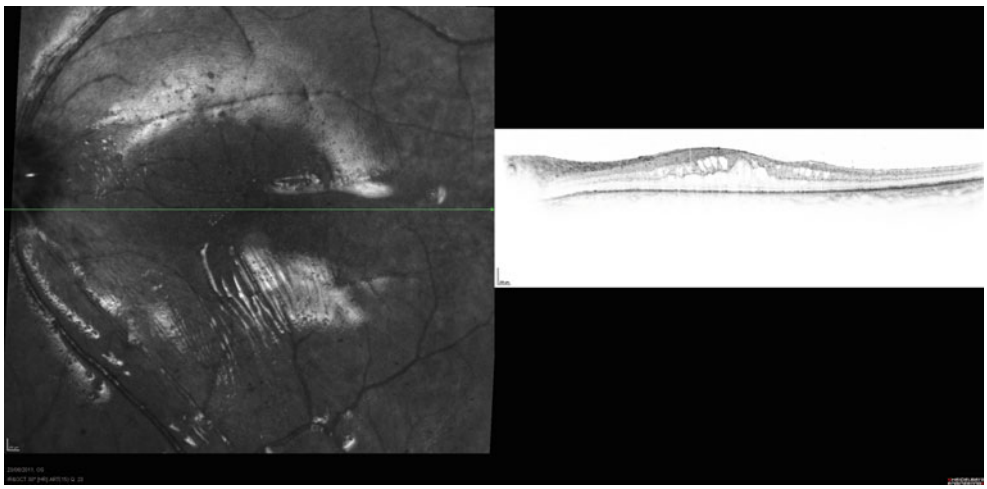

Fig. 16.32 Despite reattachment of the retina in this patient with ARN, there is CMO of the macula

litis. Intravitreal antiviral, for example, foscarnet, can be inserted during biopsy (Perez-Blazquez et al. 1997; Immonen et al. 1989).

Management of retinal detachment requires PPV, gas, laser and buckle depending on the situation (Immonen et al. 1989; McDonald et al. 1991; Blumenkranz et al. 1988, 1989). Insertion of silicone oil is often necessary because a causative single break is frequently difficult to identify; large areas of the retina are thinned and damaged, and proliferative retinopathy is common (Ahmadieh et al. 2003). Retinal attachment after multiple procedures is common (90 %) and visual recovery is poor (McDonald et al. 1991).

16.3.3 Visual Outcome

The prognosis for vision is poor in the affected eye; therefore, systemic therapy is essential to prevent involvement of the other eye.

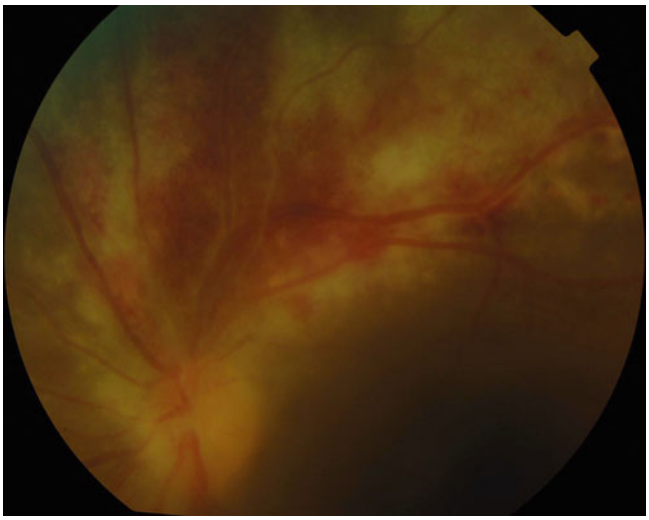

Fig. 16.33 CMV retinitis has become less common since the commencement of HAART therapy but may still be seen in immunocompromised individuals

16.4 Cytomegalovirus Retinitis

16.4.1 Clinical Features

Cytomegalovirus (CMV) infects the retina in immunocompromised patients. Overwhelmingly these patients suffer from AIDS. Prior to highly active antiretroviral therapy (HAART) (Jabs 1995), 40 % of AIDS patients developed CMV retinitis. Others requiring systemic immunosuppression such as Wegener's granulomatosis or rheumatoid arthritis are occasionally present (Akpek et al. 1999a; Fraenkel et al. 1995). Classically in AIDS, the patient has a severe reduction in CD4 white blood cells to less than 50 cells/μl. With the introduction of HAART, control of viral load is much improved, and consequently CD4 counts are more often preserved. This has led to a massive reduction in the numbers of new cases of retinitis which may only occur when there is failure of or resistance to HAART (Uphold et al. 1998; Mitchell et al. 1999; Mocroft et al. 2000; Jalali et al. 2000). Retinal detachment was a common complication of the retinitis before HAART (50 % at 1 year after development of retinitis (Jabs 1995; Jabs et al. 1991)), usually slow in onset because of the presence of a formed and attached vitreous gel in these young patients, and bilateral in 70 % (Sidikaro et al. 1991). Prior to HAART, this was linked to early mortality at approximately 6 months (Dugel et al. 1991; Irvine et al. 1997). Since HAART, patients with CMV retinitis have shown 81 % reduction in mortality (Kempen et al. 2003) and 60 % reduction in retinal detachment (Kempen et al. 2001), but most with CMV retinitis will develop a condition called immune recovery uveitis which can reduce vision (Holbrook et al. 2003; Arevalo et al.

2003; Song et al. 2003). This is characterised by posterior segment inflammation which causes secondary complications such as cystoid macular oedema (Irvine et al. 1997), vitreomacular traction (Canzano et al. 1998), vitreous haemorrhage from retinal neovascularisation (Wright et al. 2003), and even activation of previously quiescent infections of the retina such as mycobacteria (Zamir et al. 2002).

Note: Immune recovery uveitis is usually self-limiting causing only mild visual loss.

Increasingly, the control of the viral load is most important to the control of the retinitis by allowing cessation of anti-CMV therapy as the CD4 count recovers (Wright et al. 2003).

16.4.2 Surgery

Table 16.3 Difficulty rating for surgery for CMV retinitis

Difficulty rating	Moderate
Success rates	Moderate
Complication rates	Low
When to use in training	Middle

16.4.2.1 For Diagnosis

The retinal appearance is usually typical in the 'at risk' patient with a necrotising, haemorrhagic retinitis with a sharp demarcation between healthy and affected retina. However, biopsy is required to allow targeted therapy. An intravitreal biopsy of 0.2 ml is adequate for the detection of viral PCR for CMV.

16.4.2.2 For Treatment

Treatment of retinitis involves intravitreal antiviral often in the form of a slow-release Gancyclovir implant. This contains 4.5 mg of Gancyclovir, is inserted into the pars plana at 4 mm from the corneo-scleral limbus and may last up to 1 year. The implant provides local drug delivery bypassing the blood ocular barrier with low dosage whilst minimising systemic side effects. In approximately 12 %, problems are encountered such as extrusion, vitreous haemorrhage or CMO (Lim et al. 1999; Guembel et al. 1999). Endophthalmitis occurs in 0.4 % (Shane and Martin 2003).

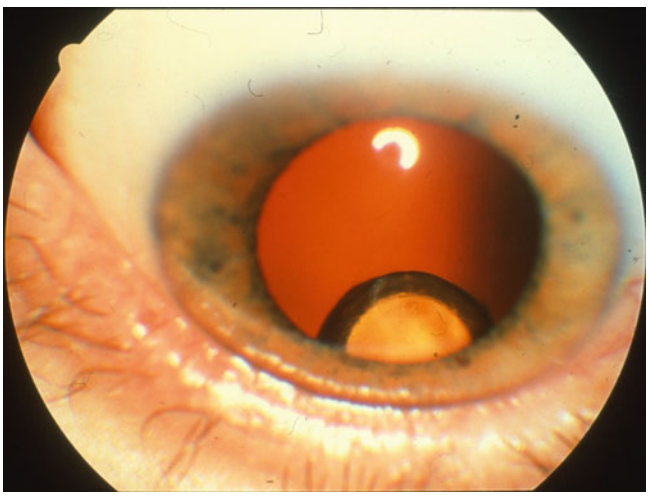

Fig. 16.34 A ganciclovir implant is visible in this eye with cytomegalovirus retinitis

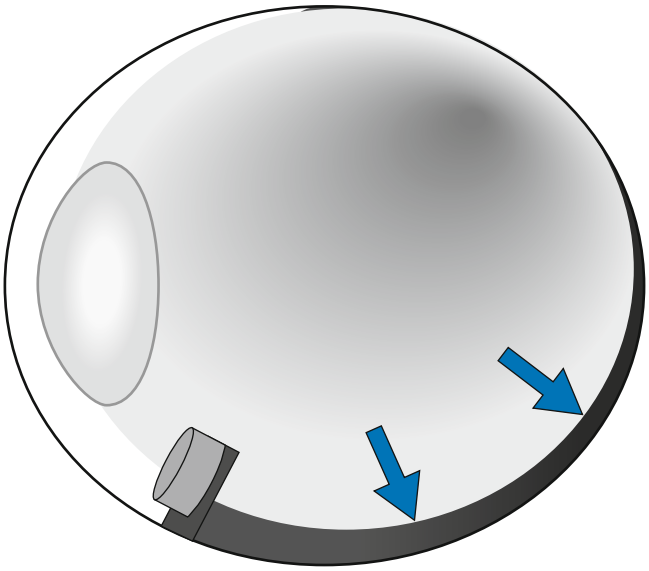

Fig. 16.35 Ganciclovir implants can be used in patients with silicone oil insertion. It is expected that there will be a higher concentration of the drug on the retina because of the thinner layer of the vitreous cavity aqueous fluid for the drug to dissolve in (*arrows*)

Implants can be used in eyes with silicone oil insertion although the reduced aqueous layer means increased concentrations of the drug (Martidis et al. 2002).

The clinical picture of retinal detachment has changed because of the use of HAART. Previously patients required PPV with silicone oil insertion without removal because of inability to destroy the CMV infection and because the shortened life span restricted the development of oil-induced complications (Dugel et al. 1991; Azen et al. 1998; Lim et al. 1994; Regillo et al. 1992). Silicone oil has been used with and without inferior external buckle with similar success rates (Nasemann et al. 1995; Garcia et al. 1995). Immune recovery means that retinitis is no longer progressive and the life span of patients is very much prolonged; therefore, surgery may be more successful with gas tamponade (Canzano et al. 1999) or with silicone oil with later removal of the oil (Schaller et al. 1999).

Attempts to restrict RRD formation or progression with prophylactic laser therapy around areas of retinitis had limited success (Althaus et al. 1998; Davis et al. 1997a; Freeman et al. 1992) because the retinitis or retinal detachment would extend through the laser barrier.

16.4.3 Visual Outcome

If retinal detachment occurs, the chance of visual recovery is better when the retina can be fixed with one operation (Scott et al. 2000), but good vision is only possible in approximately 50 % (Azen et al. 1998) although this may have improved with HAART.

16.5 Fungal Endophthalmitis

16.5.1 Clinical Features

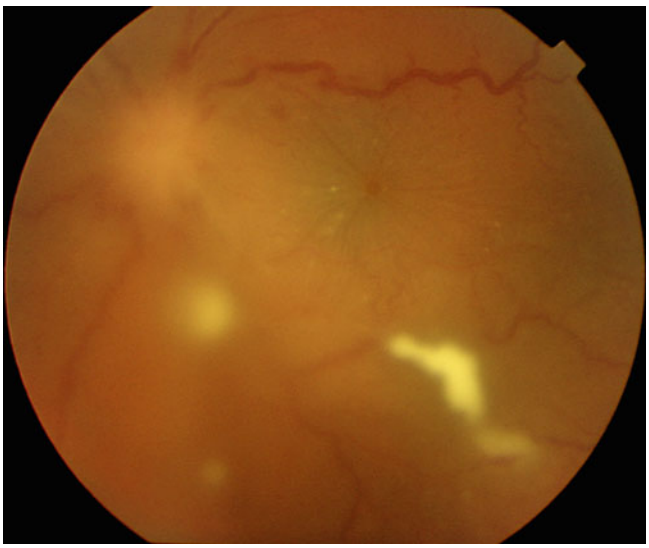

Fig. 16.36 Puff balls are seen in the mid vitreous in this patient's eye typical of *Candida* endophthalmitis

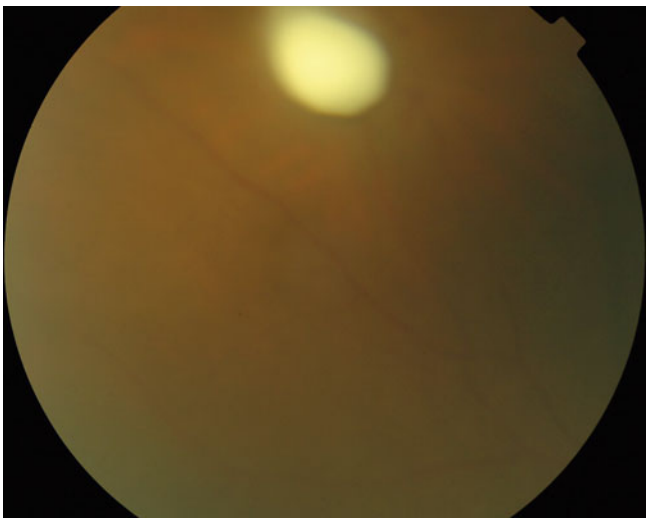

Fig. 16.37 A single focus of *Candida* in the only functioning eye of an intravenous drug abuser. The patient was treated with systemic antifungals without biopsy of the vitreous

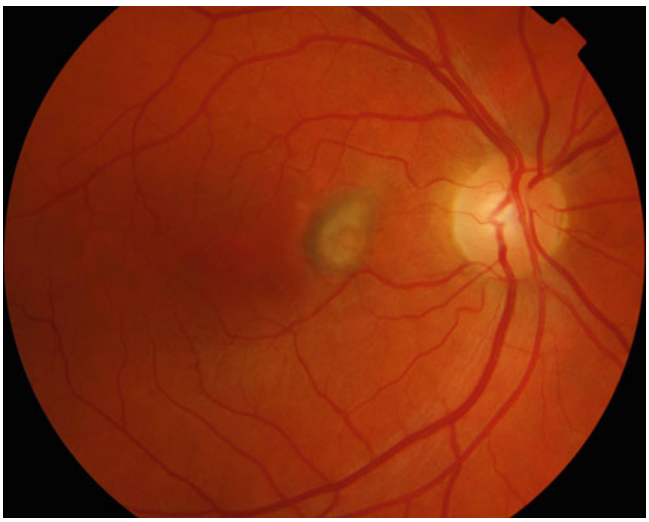

Fig. 16.38 An intravenous drug user has had *Candida* endophthalmitis in both eyes with the right producing a secondary CNV which enlarged and the left an ERM which spontaneously separated towards the disc (see Figs. 16.39–16.41)

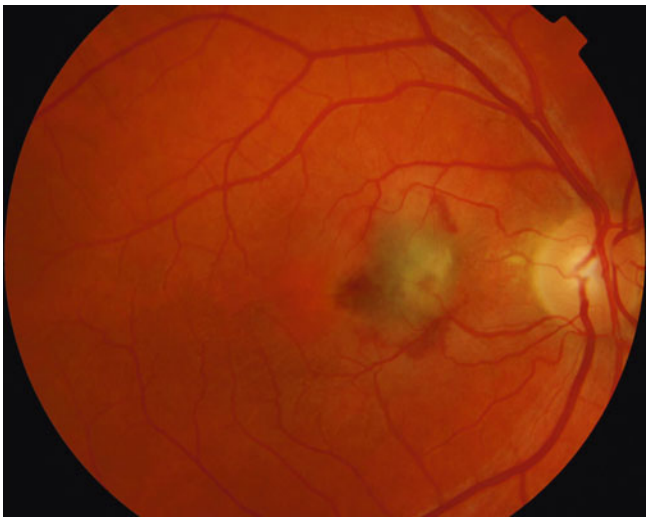

Fig. 16.39 See previous figure

Fungal endophthalmitis (predominantly *Candida albicans*) is usually seen in patients with intravenous long lines (Graham et al. 1986; Jackson et al. 2003), for example, in intensive care units, or in patients with a history of intravenous drug abuse (Aguilar et al. 1979). The presentation is a slowly progressive endophthalmitis, sometimes bilateral (Wong et al. 1997), commencing with a white spot on the retina and then preretinal puff ball infiltration often seen after routine examination of the fundus in an asymptomatic patient (Aguilar et al. 1979; Chignell 1992). An intravenous line may have been used on only one occassion (Gupta et al. 2000). In heroin abuse, the patient presents with reduction of vision after using acidic agents such as lemon juice (infected with *Candida*) to dissolve brown heroin. Infections have

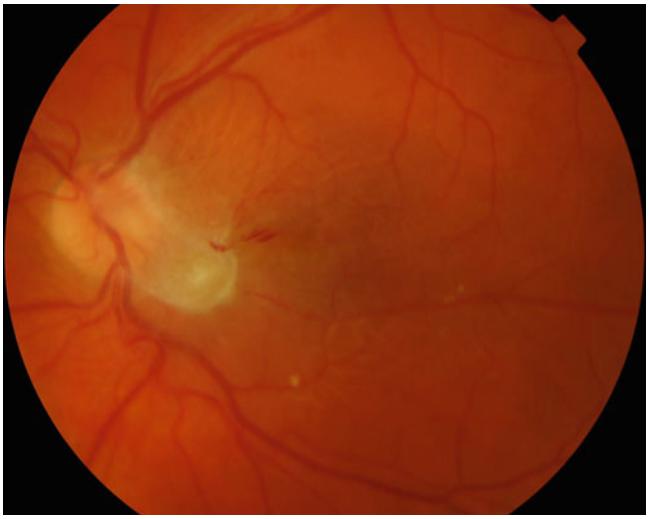

Fig. 16.40 See Fig. 16.38

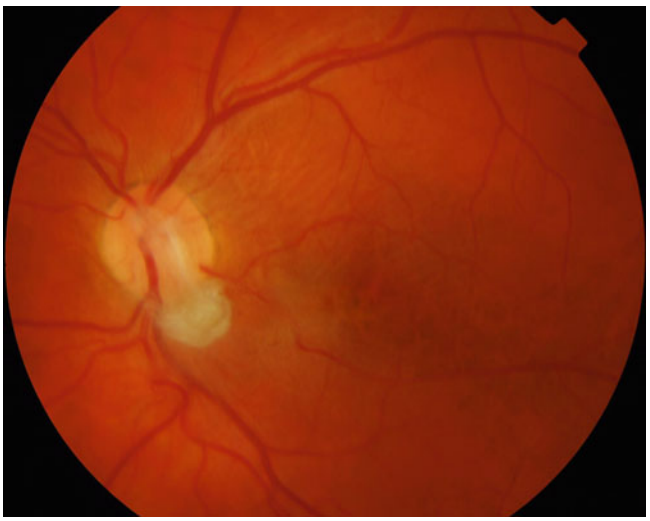

Fig. 16.41 See Fig. 16.38

been reported after gynaecological procedures (Chang et al. 2002; Chen et al. 1998), toxic megacolon (Henderson and Irfan 1996) and post-partum (Tsai et al. 2002; Cantrill et al. 1980). Premature infants may also develop the infection (Gago et al. 2002; Stern et al. 2001; Annable et al. 1990). Contaminated infusion fluid in cataract extraction caused one surgical outbreak (Sasoh et al. 1993), and the infection can be introduced during penetrating injury (Peyman et al. 1975). Otherwise exogenous infection has been described in a hop grower (Mackiewicz et al. 2000).

The infection progresses to a more severe vitreal infiltration with 'string of pearl' puffballs often with balls of whites cells on the retina if the vitreous is detached. There may be one or more foci of infiltration in the retina at the posterior pole. If untreated, epiretinal membranes may form resulting in macular pucker (McDonald et al. 1990). Retinal detachment can occur, and phthisis bulbi result (Sasoh et al. 1993).

16.5.2 Surgery

Table 16.4 Difficulty rating for PPV for *Candida* endophthalmitis

Difficulty rating	Moderate
Success rates	High
Complication rates	Low
When to use in training	Middle

16.5.2.1 For Diagnosis

Often the clinical picture is so obvious that microbiological confirmation is only confirmatory. Fundoscopy screening of intensive care patients with candidaemia can detect ocular involvement in a few percent (Rodriques-Adrian et al. 2003). Pathologically, the hyphae reside in the puff balls (Ohnishi et al. 1999). A vitreous biopsy may fail to identify the fungus because the hyphae are scanty in the vitreous. PPV with microbiological processing of the washings in the vitrectomy cassette usually yields the diagnosis, although PCR has also been advocated (Hidalgo et al. 2000; Jaeger et al. 2000). The usual agent found is *Candida albicans* and rarely others such as *Candida krusei* (McQuillen et al. 1992). Fifteen percent of cases involve *Aspergillus*, whilst *Fusarium* is rare (Essman et al. 1997).

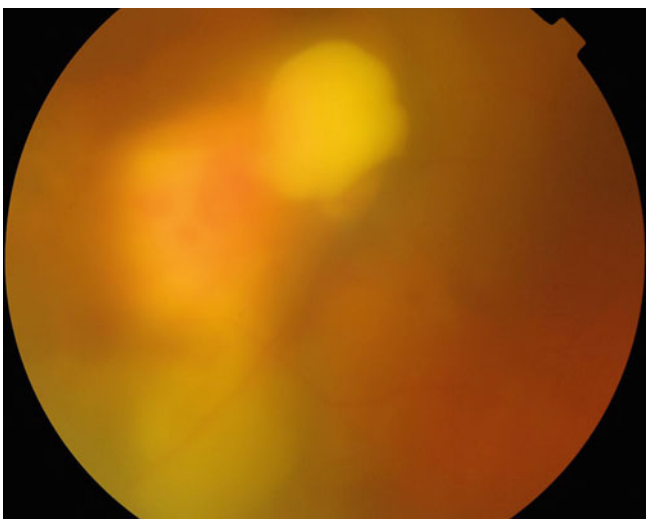

Fig. 16.42 This patient with leukaemia has developed fungal endophthalmitis from *Aspergillus*

16.5.2.2 For Treatment

The mainstay of therapy is systemic antifungal therapy (Christmas and Smiddy 1996). This will easily deal with early infection without the need for surgery and should be commenced immediately. More advanced infection with significant intravitreal infiltration requires PPV because the poor viability of the fungus in the eye will remove the local infection (Barrie 1987). This can be performed usually on the next available operating list, assuming lists every 2–3 days. Intravitreal amphotericin B is controversial because the eye will respond to systemic therapy with PPV as required (Brod et al. 1990). After vitrectomy, intravitreal amphotericin is cleared more quickly (Doft et al. 1985). In general, amphotericin is non-toxic; however, if used in too high concentration, a panuveitis occurs which will settle without loss of vision (if the injection fluid looks yellow, the amphotericin is at too high a concentration) (Payne et al. 2010).

Perform a dry vitreous biopsy at commencement of the surgery with the vitreous cutter. Many of these patients are young and therefore have an attached posterior hyaloid membrane (PHM). After core vitrectomy, the PHM should be separated from the retina. Any large focus of infiltration on the retina will usually detach the PHM without causing undue traction on the retina. Any residual white cells on the retinal surface can be aspirated. Secondary complications such as RRD or ERM can be dealt with by conventional methods.

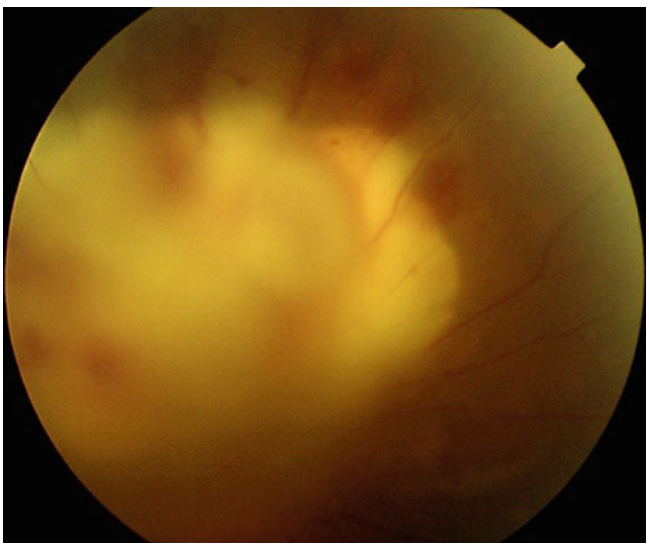

Fig. 16.43 The vitreous has been peeled from the retina in this patient with *Aspergillus* in the eye revealing a deep retinal and choroidal infiltration

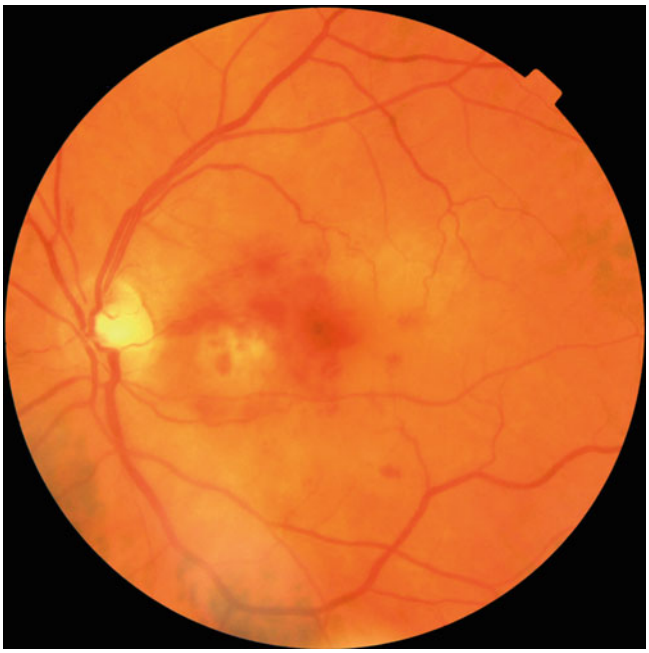

Fig. 16.44 This patient with acute myeloid leukaemia had multiple lesions in the skeletal muscles, and the liver of probable fungal aetiology was on systemic antifungal therapy. He lost vision in both eyes; the right with severe panuveitis and no fundal view and the left with a macular lesion as shown. He had right PPV and left vitreous biopsy with intravitreal amphotericin in both eyes. *Aspergillus* was confirmed on culture. The left eye recovered 20/30 vision (see Fig 16.45)

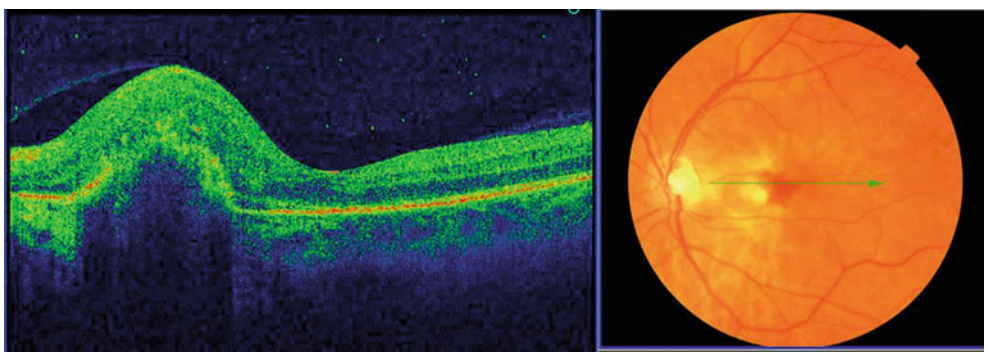

Fig. 16.45 A few months later, the patient developed a secondary CNV on the scar. The CNV responded to intravitreal anti-VEGF injection retaining 20/30 vision

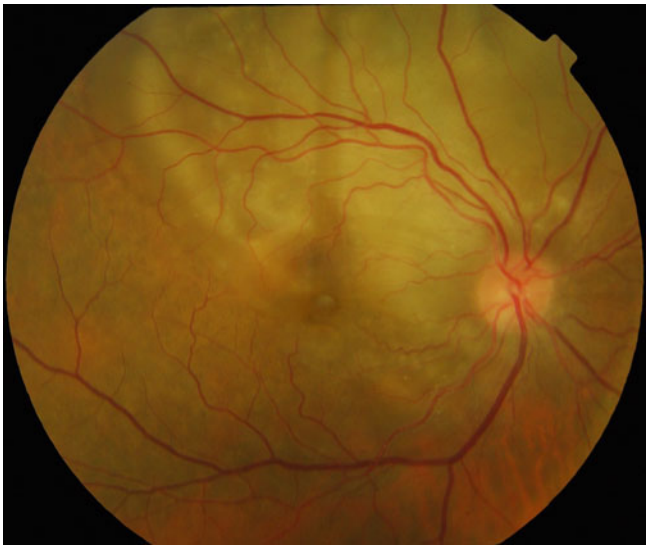

Fig. 16.46 This patient had an acute leukaemia and lost vision from a suspected fungal choroiditis. A biopsy was performed to try to detect the pathogen. A shallow RRD occurred treated with silicone oil injection and subsequent removal. The infiltration settled on systemic antifungal therapy leaving an atrophic retina and RPE in the site of the infection (see Figs. 16.47–16.48)

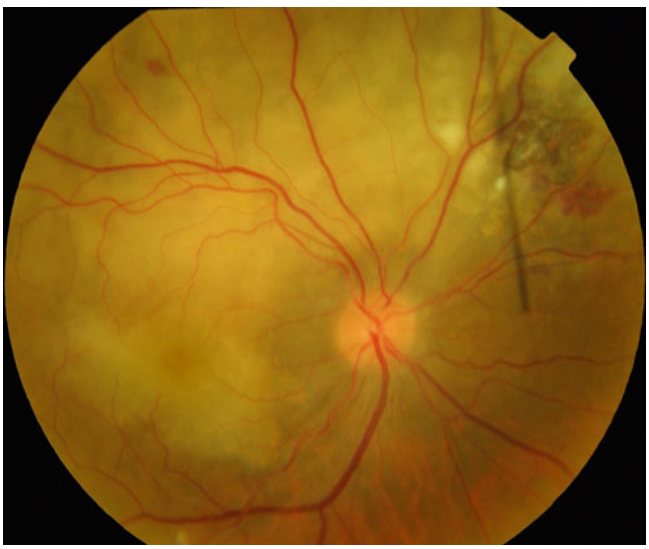

Fig. 16.47 See previous figure

16.5.3 Visual Outcome

Visual recovery depends on the severity of the infection and the location of any chorioretinal foci. In general, it is very good if the infection is dealt with early. Late presentation or diagnosis is the main reason for poor visual outcome. Visual recovery with *Aspergillus* is usually poor.

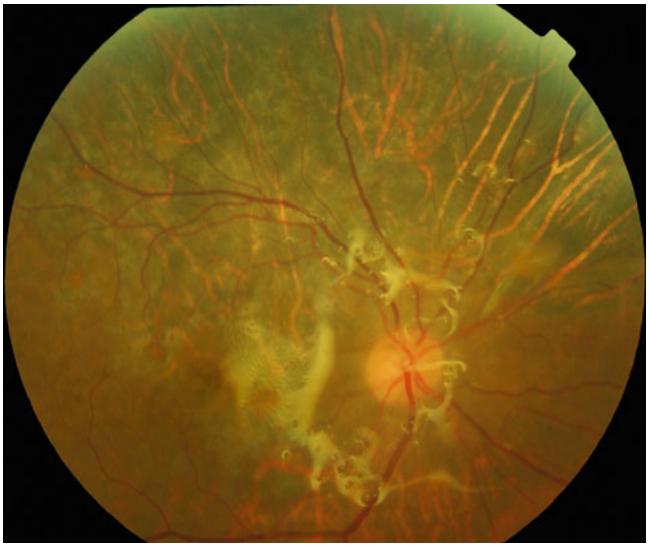

Fig. 16.48 See Fig. 16.46

16.6 Other Infections

There are other less common presentations such as toxoplasmosis (Figs. 16.50 and 16.51), which is associated with retinal detachments in approximately 6 % of cases, and Toxocara canis which may be the cause of tractional retinal detachments in childhood. Tuberculosis produces a vasculitis similar to idiopathic vasculitis and Eales' disease and can result in retinal detachment despite response to systemic therapy.

Causes of vitritis detectable by polymerase chain reaction (PCR):

- Herpes simples virus 1 and 2 (HSV 1 and 2)
- Varicella zoster virus (VZV)
- Cytomegalovirus (CMV)
- Epstein–Barr virus (EBV)
- Borrelia burgdorferi
- Toxoplasma gondii
- Mycobacterium tuberculosis
- Propionibacterium acnes
- Whipple's disease
- Ocular Lymphoma

16.6.1 Clinical Features

Biopsy for neoplasia accounts for 14 % of vitreous biopsies with 72 % of these having ocular lymphoma (Verbraeken et al. 1997).

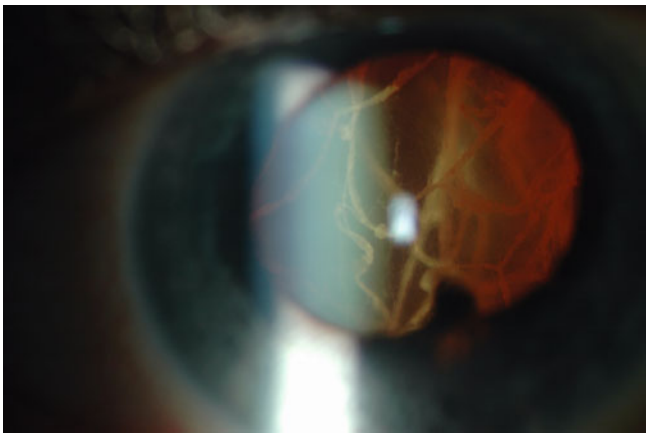

Fig. 16.49 Opacity in the vitreous is a common reason for PPV in patients with toxoplasmosis chorioretinitis

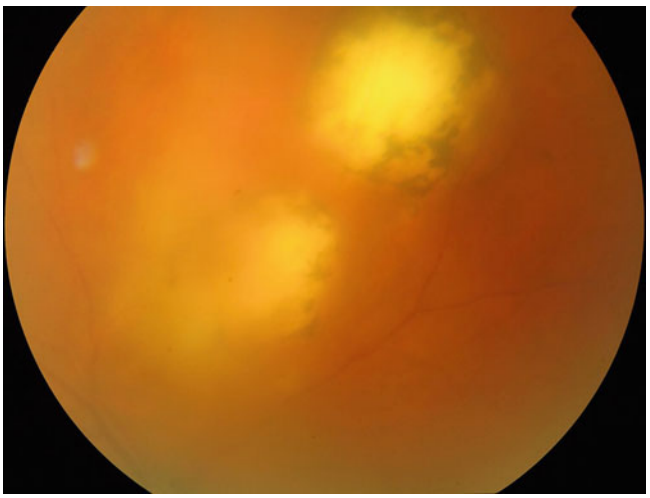

Fig. 16.50 A hazy vitreous with a toxoplasmosis scar

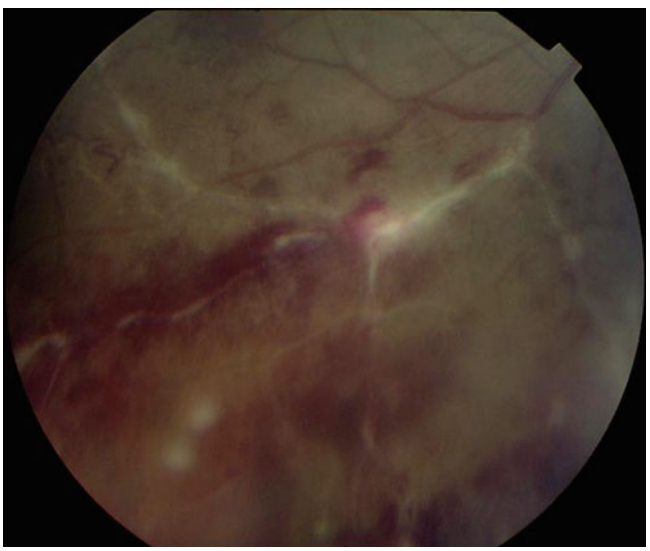

Fig. 16.51 A patient with tuberculous uveitis and a secondary vitreous haemorrhage (see Fig. 16.52)

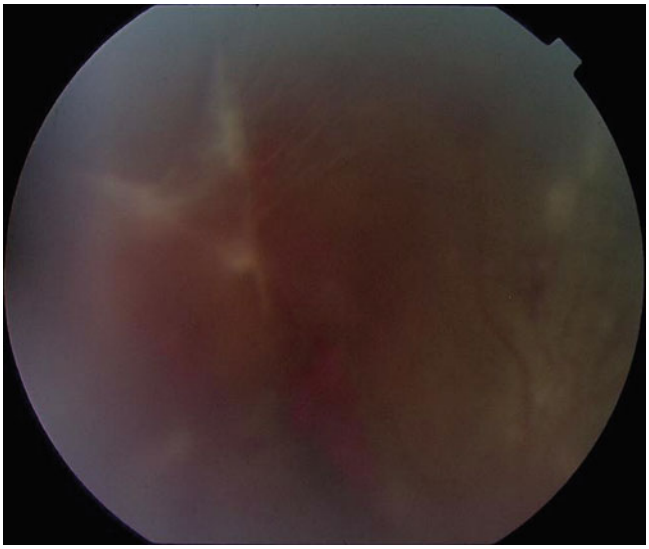

Fig. 16.52 See previous figure

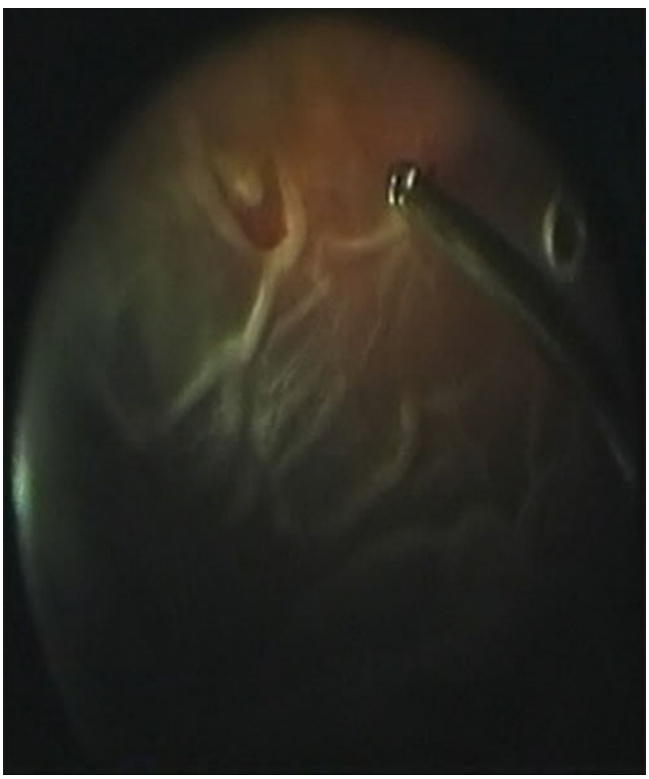

Fig. 16.53 This patient with tuberculosis and retinal vasculitis has developed a retinal tear and a retinal detachment

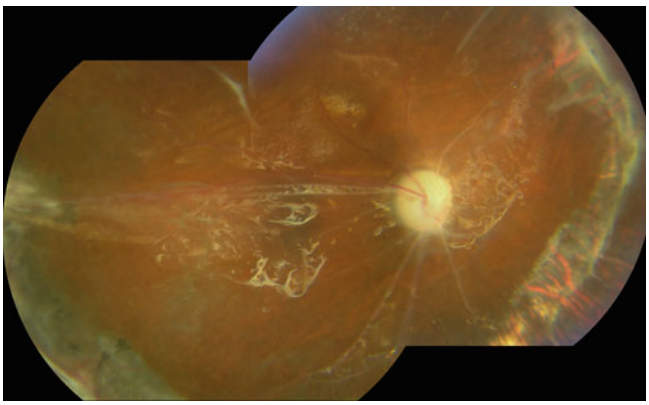

Fig. 16.54 This patient with tuberculosis retinitis and RRD required a PPV, 360° retinectomy and silicone oil insertion into the right eye and PPV and gas on the left with visual recovery of counting fingers on the right and 20/30 left after systemic antitubercle therapy (see Fig. 16.55)

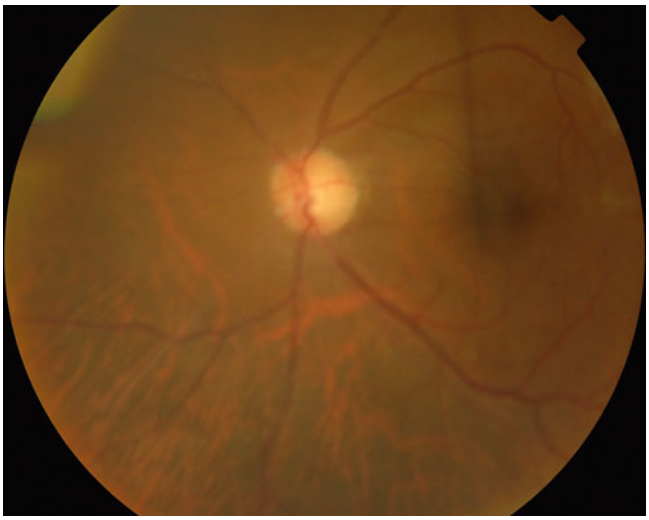

Fig. 16.55 See previous figure

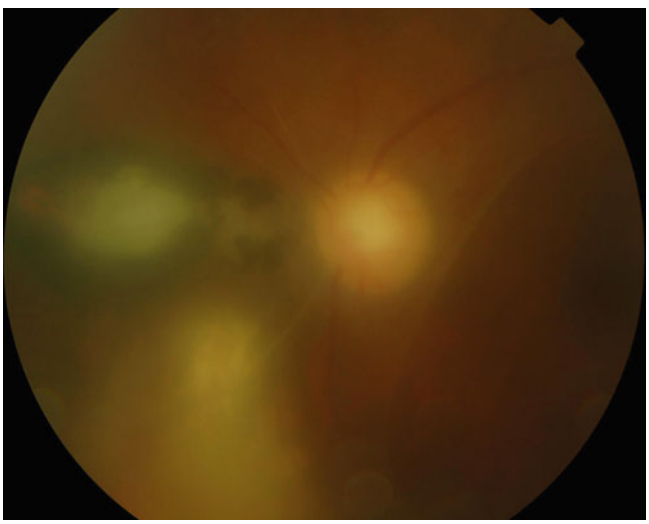

Fig. 16.56 Vitrectomy may be used to remove vitreous debris in ocular toxoplasmosis

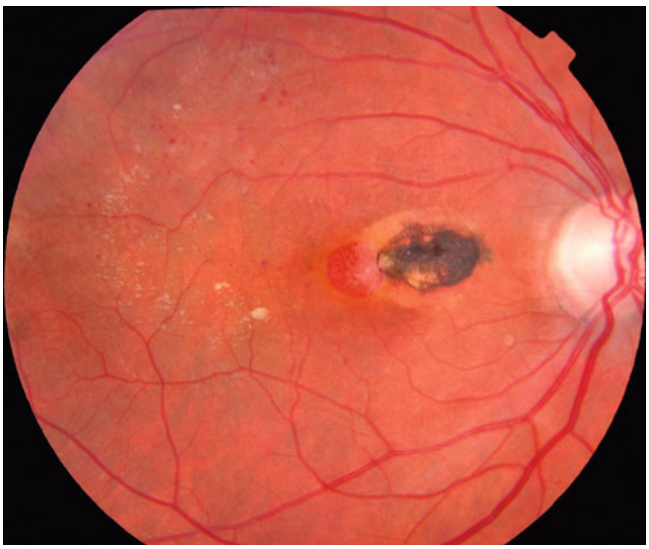

Fig. 16.57 This patient with congenital macular scars from toxoplasmosis developed a macular hole on the edge of the scar in the right eye which unfortunately did not close after surgery (see Fig. 16.58)

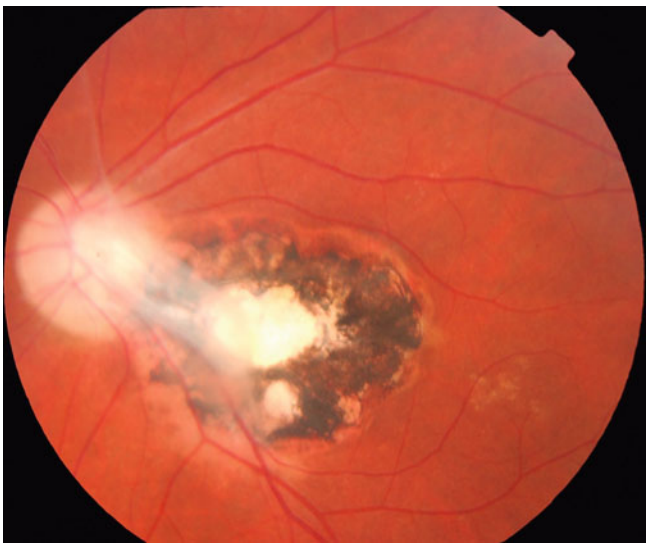

Fig. 16.58 See previous figure

Lymphoma in the eye presents in the elderly, often female and often bilaterally (Palexas et al. 1995). Ocular lymphoma should be considered in a patient with steroid resistant posterior uveitis (Peterson et al. 1993). The clinical features however can be vague and varied with intravitreal white cells in a quiet eye, subretinal infiltration and occasional haemorrhagic retinal necrosis (Akpek et al. 1999b; Ridley et al. 1992). Pseudohypopyon can occur (Lobo et al. 2003). 50 % of cases present because of ocular symptoms or signs; the rest because of CNS involvement (20 % of CNS lymphoma will affect the eye) (Peterson

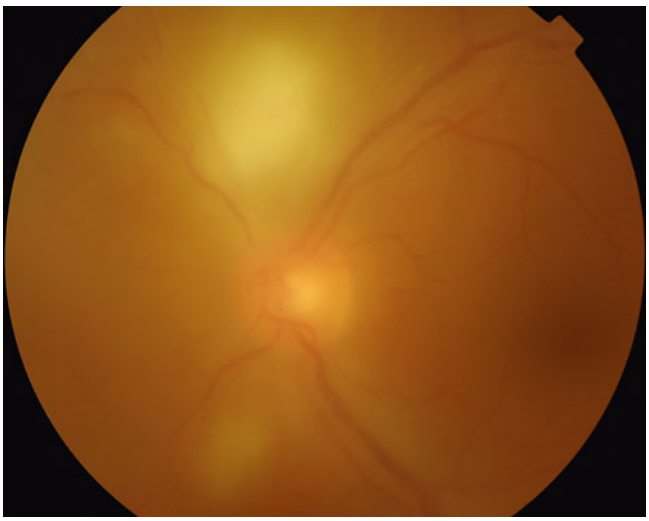

Fig. 16.59 This patient with posterior uveitis received intravitreal steroid which caused an exacerbation of the uveitis; a diagnosis of toxoplasmosis was subsequently made on vitreal biopsy and PCR testing

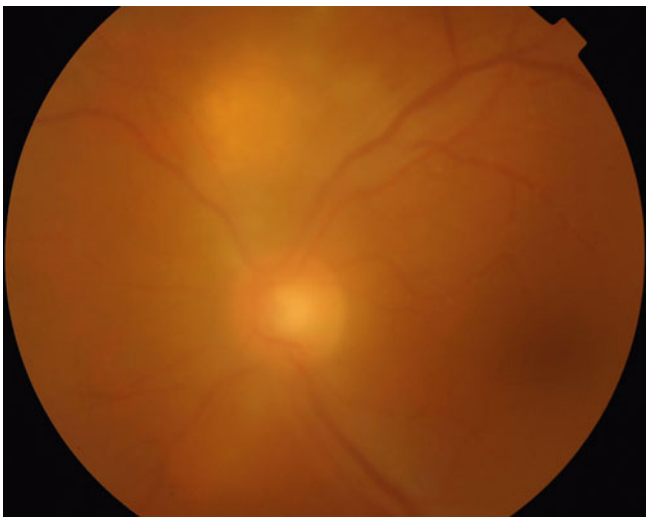

Fig. 16.60 After treatment of the toxoplasmosis, the inflammation began to subside

et al. 1993; Herrlinger 1999). Usually a diffuse large cell B-cell lymphoma is implicated (Coupland et al. 2003). Epstein–Barr virus has been implicated in patients with AIDS, but biopsy samples are often positive for this virus without evidence of infection (Batara and Grossman 2003; Rivero et al. 1999; Mittra et al. 1999).

Investigation for systemic or intracerebral lymphoma is advised. Low-dose radiotherapy is very effective in reducing infiltration in these eyes (Margolis et al. 1980), and systemic chemotherapy may be considered (Akpek et al. 1999b).

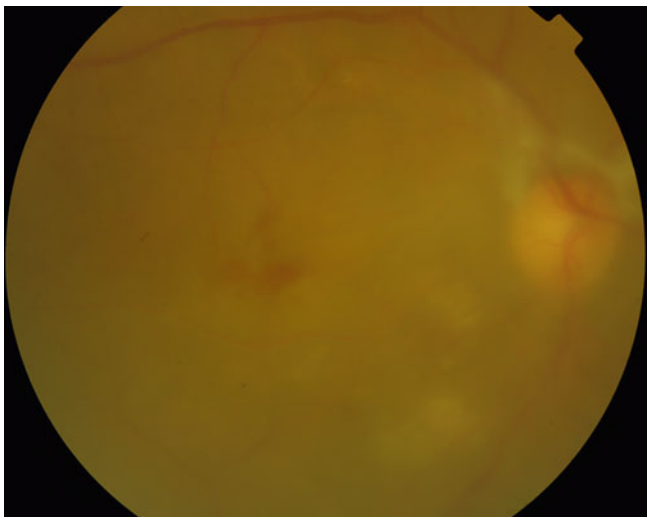

Fig. 16.61 Images are shown of a patient with tuberculous panuveitis. This patient developed bilateral RRD

Table 16.5 Cytology of the vitreous in infectious and non-infectious uveitis

Non-infectious uveitis	
Lymphoma	Atypical lymphocytes
Leukaemia	Atypical lymphoid cells
Metastatic tumour	Tumour cells
Melanoma	Tumour cells with melanin
Inflammatory uveitis	Inflammatory cells (plasma cells, lymphocytes, polymorphonuclear leucocytes, monocytes)
Lens-induced uveitis	Lens material, inflammatory multinucleate cells or phacolytic cells
Epithelial down growth	Fibroblasts
Amyloidosis	Acellular globules
Juvenile xanthogranuloma	Histiocytes, Touton giant cells
Infectious uveitis	
Bacteria	Bacteria, neutrophils
Mycobacteria	Acid-fast bacilli
Fungal	Yeast, hyphae, mononuclear cells
Toxoplasmosis	Tachyzoites
Toxocariasis	Eosinophilia, plasma cells, second-stage larvae
Acute retinal necrosis	Inflammatory cells
Viral infections	Mononuclear cells

16.6.2 Surgery

Table 16.6 Difficulty rating for PPV for ocular lymphoma

Difficulty rating	Moderate
Success rates	Moderate
Complication rates	Low
When to use in training	Middle

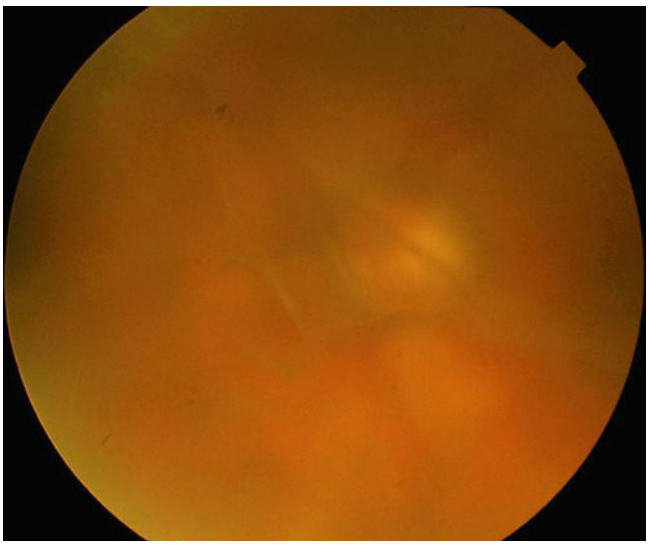

Fig. 16.62 This patient has intraocular lymphoma. This is often characterised by diffuse white cell infiltration in a non-specific manner. Clinically, the diagnosis may be difficult to discriminate from other types of uveitis

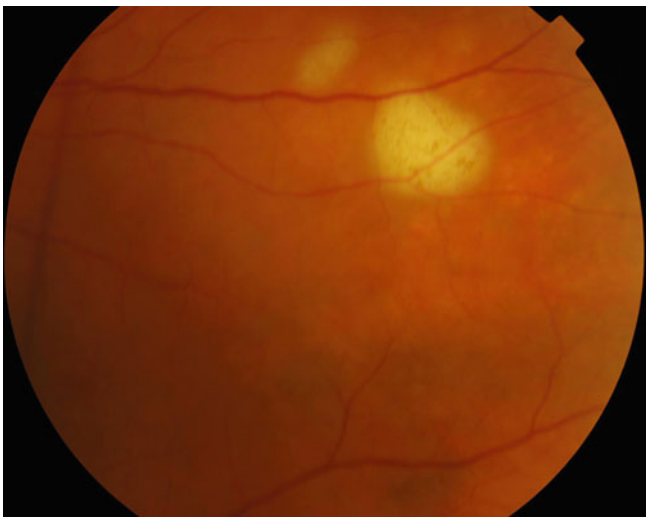

Fig. 16.63 Subretinal infiltrates are typical of intraocular lymphoma

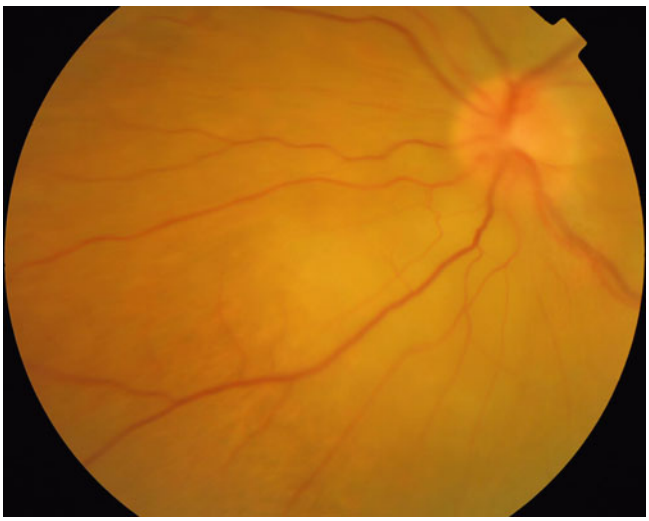

Fig. 16.64 A rare presentation of lymphoma with diffuse choroidal infiltration on fundoscopy and ultrasound (see Fig. 16.65)

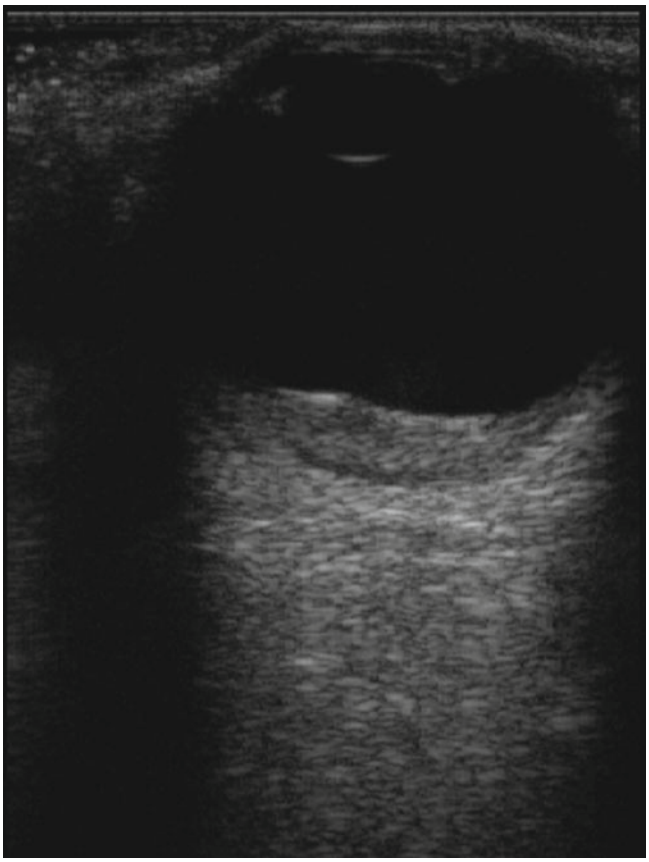

Fig. 16.65 The same patient's ultrasound demonstrating the degree of thickening

16.6.2.1 For Diagnosis

A vitreous biopsy should be taken but requires rapid processing of the sample (Verbraeken et al. 1997; Whitcup et al. 1993) because the lymphoma cells are fragile and barely viable . Often cytology fails to identify the cells, and differentiation from inflammation is difficult. Immunotyping to identify monoclonal cell lines is useful to overcome the latter problem (Davis et al. 1997b).

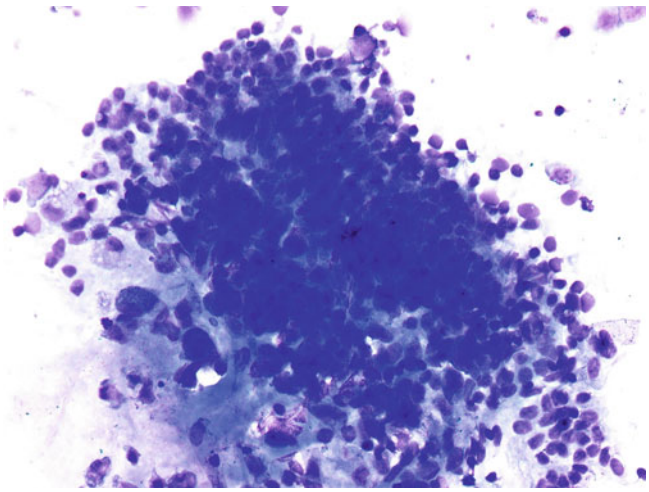

Fig. 16.66 Cytology can be performed, but vitreous samples must be processed immediately to prevent loss of fragile lymphomatous cells

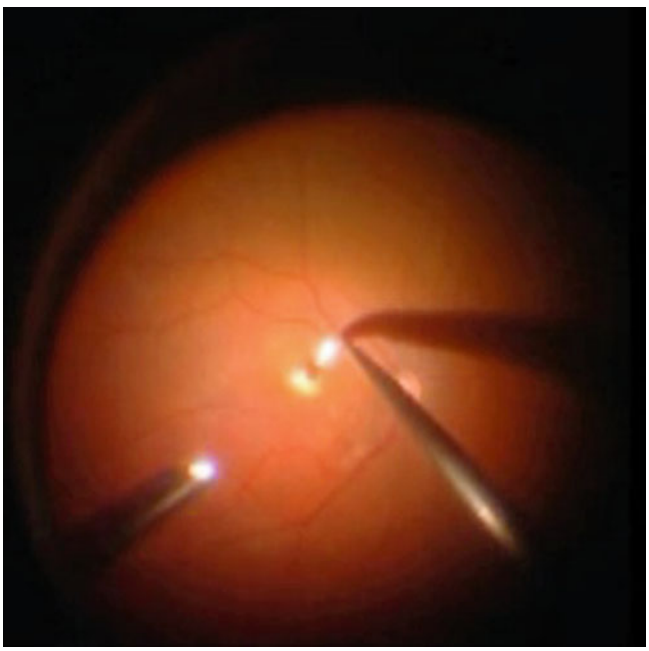

Fig. 16.67 Subretinal infiltrates in suspected ocular lymphoma are a good source of cells for diagnostic confirmation. These can be aspirated via a retinotomy

16.6.2.2 Chorioretinal Biopsy

Other options that have been employed include retinal biopsy (Coupland et al. 2003) or aspiration of subretinal infiltrates (Ciulla et al. 1997). These provide higher yields because the cells are more viable than in the vitreous.

- Chose an area of the retina approximately 2–3 disc diameters affected by infiltration that is superior and mid-peripheral away from large blood vessels.
- Surround the biopsy site with confluent diode laser prior to excision (or if not available use endodiathermy burns) to close the choroidal blood vessels.
- Use vertical cutting scissors to cut through the centre of the burns incising both the choroid and retina.
- Remove the block of tissue with forceps through a sclerotomy; you will need at least a 20-gauge sclerotomy. Take care that the choroid and retina can separate from each other during extraction; the retina is usually fairly tough and is easily kept hold of, but the choroid can be washed away by fluid coming out of the sclerotomy. Inspect the tissue to check that you have both layers; search on the drape on the cheek of the patient if the pigmented choroid has been washed off!
- Laser around the site of excision.
- Insert long-acting gas to maintain a flat retina.

Chorioretinal biopsy is usually reserved for those eyes with poorer visual potential. Subretinal cells from a subretinal deposit can be aspirated through a small-gauge cannula inserted via a retinotomy.

Intraocular methotrexate can be inserted in resistant cases (Valluri et al. 1995).

Samples can be examined by flow cytometry.

16.6.2.3 For Treatment

Surgery is performed either for restoration of vision because the vitreous cells are reducing vitreal clarity. PPV can be used to clear the visual axis and is usually uneventful. Intravitreal methotrexate can be injected to reduce the local response in the eye.

16.6.3 Visual Outcome and Survival

The prognosis for visual recovery is good. These lymphomas do not usually spread systemically. However, the patients have a shortened life expectancy due to the development of intracerebral lymphoma resulting in a poor duration of survival for these patients of median 3 years (Batara and Grossman 2003).

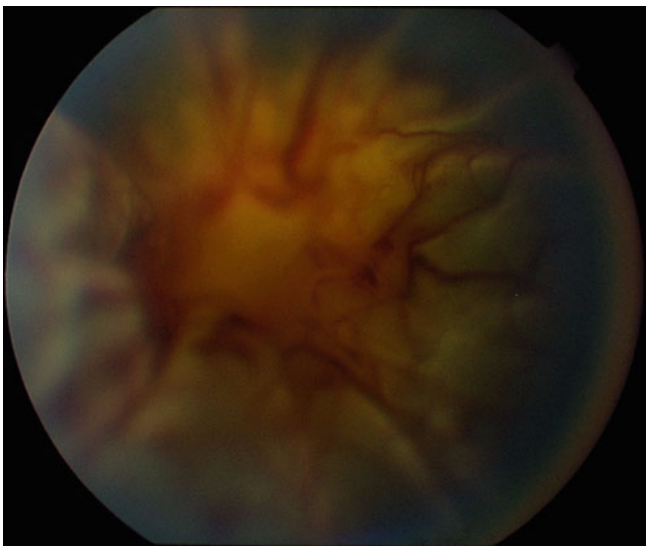

Fig. 16.68 An acute relapse of acute lymphocytic leukaemia in this patient was accompanied by an exudative retinopathy

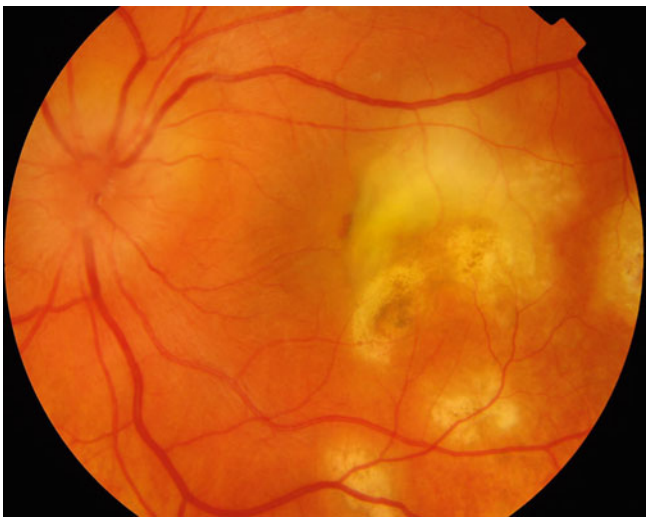

Fig. 16.69 In some patients despite vitreous, retinal and choroidal biopsy, a definitive diagnosis is not reached. This patient had poor vision because of optic nerve involvement and also had a CNV on the edge of scarring

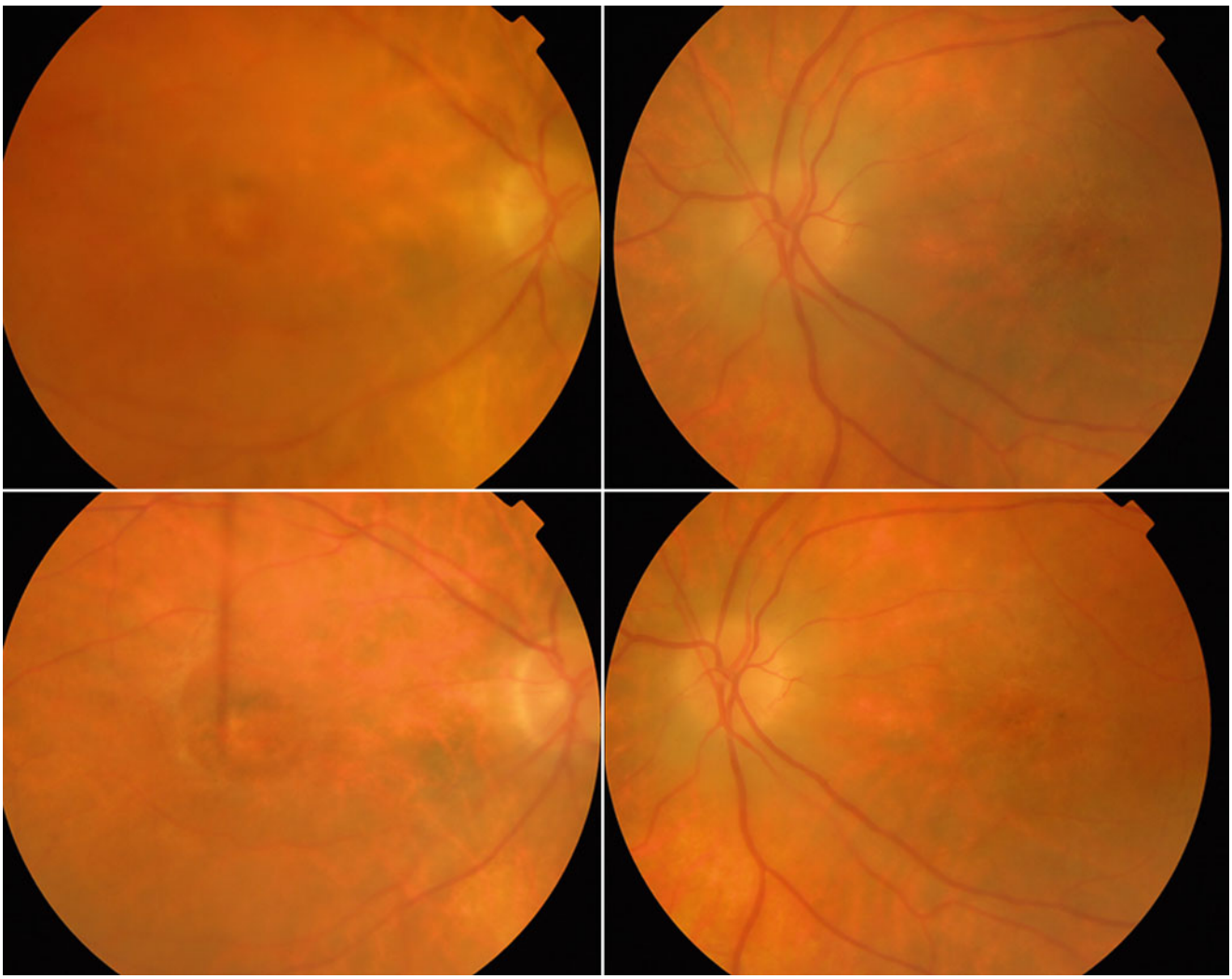

Fig. 16.70 A panuveitis with the development of macular changes and optic atrophy associated with the CRMP 5 gene and a small cell carcinoma. A retinal biopsy was performed to try to aid the diagnosis

16.7 Paraneoplastic Retinopathy

Patients with carcinoma or melanoma may present with severe loss of vision with a non-specific panuveitis (Lu et al. 2009). Loss of vision occurs centrally with scotomas and photopsia. Antibodies to retinal proteins can be detected. A systemic workup and investigation are required if the source of the neoplasia is unknown. Suspect this rare diagnosis in a patient with diffuse non-specific retinal changes but severe loss of vision.

16.8 Summary

Vitreoretinal methods can be adapted to aid diagnosis and treatment of a wide variety of uveitic, infectious and neoplastic conditions. All have their own hazards surgically, and most often other specialties both ophthalmological and otherwise become involved in the care of the patient.

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